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CHEMISTRY OF FOOD AND NUTRITION

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CHEMISTRY
OF
FOOD AND NUTRITION

BY

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PREFACE

THE purpose of this book is to present the principles of the chemistry of food and nutrition with special reference to the food requirements of man and the considerations which should underlie our judgment of the nutritive values of foods. Food is here considered chiefly in its relations to nutrition, the more detailed description of individual articles of food and the chemical and legal control of the food industry having been treated in another volume.

The present work is the outgrowth of several years' experience in teaching the subject and is published primarily to meet the needs of college classes. It is hoped that the book may also be of service to other readers who appreciate the importance of food and nutrition as factors in health and are interested in the scientific foundations which have been so greatly broadened and strengthened by the investigations of the past few years.

While the small size, to which the book is limited by its main purpose, permits little of either historical or technically critical treatment, yet a limited number of original investigations and of controverted views have been discussed in order to give an idea of the nature of the evidence on which our present beliefs are based, and in some cases to put the reader on guard against theories which, while now outgrown, are still sometimes encountered.

Special attention has been given to the difficult task of attempting to present the striking results of some of the most recent investigations in nutrition in such a manner as to make clear their importance without giving exaggerated impressions and with due emphasis upon the fact that on many significant points any interpretation which can now be offered is necessarily tentative. It is hoped that study of the text will be supplemented by consultation of the references suggested at the close of each chapter, which should serve to put the reader in touch with much of the more significant literature and make him familiar with the scientific journals in which the future developments of this rapidly growing subject may be followed as they appear.

The author desires to express his indebtedness to the colleagues and former students who have contributed many helpful suggestions and specifically to Doctors A. W. Thomas and M. S. Rose, Miss L. H. Gillett and Miss H. M. Pope for valuable criticism and assistance in the preparation of the present revision of the work.

H. C. S.

NOVEMBER, 1917.

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INTRODUCTION

THE activities on which the life of the body depends involve a continuous expenditure of energy and a constant exchange of material. Ultimately the body is dependent upon food for the fuel materials which supply energy and for both the substances which are transformed in, and eliminated from, the body, and those whose presence regulates and controls these transformations. The materials leaving the body are to be regarded not merely as wastes but as end products of an orderly and coordinated series of chemical reactions which occur in the body and by virtue of which its functions are performed. Thus the chief functions of food are: (1) to yield energy, (2) to build tissue, (3) to regulate body processes.

These functions involve reactions which are dependent upon the chemical composition and constitution of the food. Any food constituent which takes part in any of these functions may be regarded as having nutritive value.

Most of the nutrient material contained in food requires more or less change to bring it into the exact forms most useful in nutrition. These changes as a rule take place in the digestive tract and together constitute the process of digestion.

The changes which take place in the foodstuffs, after they have been absorbed from the digestive tract, are included under the general term "metabolism." Although the chemical changes and the energy transformations are of course inseparable, it has become customary to speak of the metabolism of matter and the metabolism of energy, and to regard the extent of the metabolism of any material substance as measured by the amount of its end products eliminated, and the extent of the energy metabolism as measured by the amount of heat, or of heat and external muscular work, which the body gives off.

The metabolism of matter and the metabolism of energy are normally supported by the food; but if no food is taken, they continue at the expense of the body substance. The expenditure of energy can never cease in the living body because it includes the work involved in carrying on the internal processes which are essential to life itself; and the expenditure of matter cannot cease because the energy for this necessary work is obtained by the breaking down of the organic compounds of the food or of the body substance into simpler compounds, many of which are of no further use to the body and must be eliminated. When the food supplies sufficient energy, the body substance is protected; when the food is insufficient, body substance is burned as fuel. In order, then, to consider intelligently the nutritive requirements of the body as regards the substances of which it is composed, it is necessary first to know whether the fuel requirements (the requirements of the energy metabolism) have been fully met.

The carbohydrates, fats, and proteins of the food all serve as fuel to yield the energy required for the activities of the body, and the proteins serve also as material for the maintenance or growth of body tissue. But of the fifteen chemical elements which are essential to the structure and functions of the body, simple proteins furnish only five. The remaining ten elements are largely constituents of the ash of the food and are known as ash constituents, inorganic foodstuffs, mineral matter, or salts.

Recent investigations have developed the fact that food of sufficient energy value and containing ample amounts of each of the chemical elements known to be essential to the body is not necessarily adequate to meet all the requirements of nutrition. Thus it appears that certain substances occurring in natural foods but not yet chemically identified are also to be included among the nutritive requirements of the body and therefore among the factors which determine the nutritive values of foods. At present these unidentified substances are referred to as "vitamines" or as "fat soluble A" and "water soluble B."

The essentials of a chemically adequate food supply may therefore be summarized as follows: (1) sufficient of the organic nutrients in digestible forms to yield the needed energy; (2) protein, sufficient in amount and appropriate in kind; (3) adequate amounts and proper proportions of the various ash constituents or inorganic foodstuffs; (4) sufficient of each of the two unidentified "vitamine" factors, the "fat soluble A" and the "water soluble B."

In attempting to give in the following pages a general view of the chemistry of food and nutrition it has seemed best to discuss first the chemical nature and nutritive functions of the substances which serve as sources of energy in nutrition, then the nutritive requirements in terms of energy, protein, the more prominent "inorganic" elements, and the "vitamines," and finally the bearing of these various factors of food value upon problems connected with the economic use of food.

CHEMISTRY OF FOOD AND NUTRITION

CHAPTER I

CARBOHYDRATES

Of the constituents of the ordinary mixed food of man the carbohydrates are usually the most abundant and the most economical sources of energy. They are also considered to be the first of the three great groups of foodstuffs to be formed by synthesis from simple inorganic substances in plants; "in the long run, all the energy of living matter comes from them." The synthesis of carbohydrates in nature is therefore a logical starting point for the study of the organic foodstuffs.

In the chlorophyll cells of the leaves of green plants the energy of the sun's rays brings about reaction between carbon dioxide and water which results in the liberation of oxygen and the formation of organic compounds. There is still doubt as to the exact mechanism of the process and no certainty that it is the same in all cases. It has, however, been quite generally found that the volume of oxygen liberated is equal to that of carbon dioxide consumed. The simplest possible representation of the reaction would be

$$CO_2 + H_2O \rightarrow CH_2O + O_2$$

according to which the first product of the synthesis would be formaldehyde. There is considerable (though not conclusive) evidence that formaldehyde is thus formed and that it is rapidly built up into less reactive compounds. Whatever the steps in the process* there is normally an early production of carbohydrate. Usually the first product which can be demonstrated as accumulating in the plant as the result of the photosynthesis is a sugar (glucose or sucrose) or starch. Assuming glucose as a typical product and neglecting the intermediate stages, the photosynthesis of carbohydrate may be represented thus:

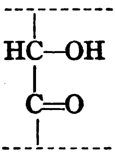
$$6\ CO_2 + 6\ H_2O \rightarrow C_6H_{12}O_6 + 6\ O_2$$

Glucose is the most familiar representative of a group of simple sugars (monosaccharides or monosaccharoses) which are in composition direct polymers of formaldehyde (CH_2O) and which are classified, according to the number of carbon atoms in the monosaccharide molecule, as trioses, pentoses, hexoses, etc.

Classification

Definitions of the term " simple sugar " vary somewhat, depending chiefly upon the views of different authors as to how simple a compound may properly be called a sugar.

According to Browne, a simple sugar or monosaccharide may be defined as an aldehyde alcohol or ketone alcohol of the aliphatic series, the molecule of which contains one carbonyl and one or more alcohol groups, one of the latter being always adjacent to the carbonyl group. All simple sugars contain, therefore,



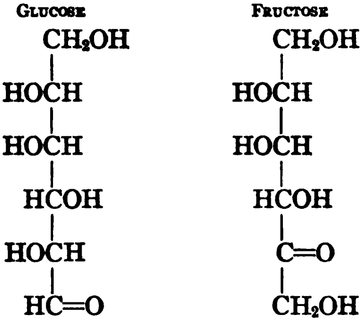
$$\begin{array}{c} \text{- - - - - - - - - -} \\ | \\ HC{-}OH \\ | \\ C{=}O \\ | \\ \text{- - - - - - - - - -} \end{array}$$

---

* For concise discussion of the synthesis of carbohydrates in plants the reader may be referred to Armstrong's *The Simple Carbohydrates and the Glucosides*, pages 92–96; Browne's *Handbook of Sugar Analysis*, pages 532–534; and Mathews' *Physiological Chemistry*, pages 44–49. A somewhat fuller account will be found in Jost's *Pflanzenphysiologie* and Euler's *Pflanzenchemie*, and a very detailed treatment of the subject in Czapek's *Biochemie der Pflanzen*. For discussion from a more physiological standpoint, see Pfeffer's *Plant Physiology* and summary of recent work by Jorgenson and Stiles in *The New Phytologist*.

as a characteristic group upon the presence of which the chief chemical properties of the sugars depend.

The simplest possible sugar according to this definition is glycolaldehyde, $CH_2OH—CHO$, which (in analogy with the nomenclature of the familiar sugars) may also be called *glycolose.* The structural formulæ of glucose and fructose, the most familiar representatives of the aldehyde-alcohol (aldose) and ketone-alcohol (ketose) sugars, respectively, are as follows:



$$\begin{array}{c} CH_2OH \\ | \\ HOCH \\ | \\ HOCH \\ | \\ HCOH \\ | \\ HOCH \\ | \\ HC{=}O \end{array} \qquad \begin{array}{c} CH_2OH \\ | \\ HOCH \\ | \\ HOCH \\ | \\ HCOH \\ | \\ C{=}O \\ | \\ CH_2OH \end{array}$$

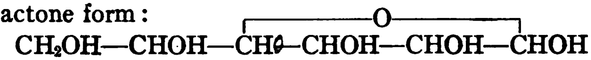
Since glucose gives aldehyde reactions but not so readily as the above structural formula would lead one to expect, it is believed that in ordinary solutions of glucose the substance exists partly in the condition indicated by the aldehyde formula and partly in a tautomeric form represented by the lactone or " oxygen bridge " formula.

Following are the aldehyde and lactone formulæ written without reference to the spatial relationships of the hydrogen and hydroxyl groups:

Aldehyde form:

$$CH_2OH—CHOH—CHOH—CHOH—CHOH—CHO$$

Lactone form:



$$CH_2OH—CHOH—\overbrace{CH—CHOH—CHOH—CHOH}^{O}$$

The name monosaccharide (" single sugar ") implies that the monosaccharide molecule contains only one sugar radicle — that it cannot be split by hydrolysis into sugars of lower molecular weight. A substance like cane sugar which on hydrolysis splits to two molecules of simple sugar is called a disaccharide or disaccharose (" double sugar "). Trisaccharides and tetrasaccharides are also known. Substances which like starch are of high molecular weight and on complete hydrolysis yield many molecules of simple sugar are called polysaccharides * or polysaccharoses.

The term " carbohydrates " covers all the simple sugars and all substances which can be converted into simple sugars by hydrolysis. The term " glucosides " is applied to substances which consist of combinations of carbohydrate radicles with radicles of other kinds and which therefore yield on hydrolysis both a simple sugar and one or more products of other than carbohydrate nature.

CLASSIFICATION OF CARBOHYDRATES †

MONOSACCHARIDES (Monosaccharoses)

Dioses ($C_2H_4O_2$) — Glycolose.

Trioses ($C_3H_6O_3$).
    Aldoses — Glycerose.
    Ketose — Dioxyacetone.

Tetroses ($C_4H_8O_4$).
    Aldoses — Erythrose,[3] Threose.[3]
    Ketose — Erythrulose.[2]

Pentoses ($C_5H_{10}O_5$).
    Aldoses — Arabinose,[2] Xylose,[2] Ribose,[2] Lyxose.[3]
    Ketoses — Araboketose[3], Xyloketose (ketoxylose).[2]
    [Methyl pentoses ($C_6H_{10}O_5$) — Rhamnose,[2] Fucose [2]].

---

* Some writers use the term polysaccharides to include all carbohydrates other than monosaccharides. Mathews applies it to all carbohydrates more complex than the disaccharides.

† Names of a few of the most important carbohydrates are printed in small capitals. Separate mention of the *d*, *l*, and *dl* forms of the various sugars is omitted, since in the study of food and nutrition we are practically concerned only with that one of the three forms which is found in or derived from natural products.

Hexoses ($C_6H_{12}O_6$).

Aldoses — GLUCOSE,[1] Mannose,[2] GALACTOSE,[2] Gulose,[3] Idose,[3] Talose,[3] Allose,[3] Altrose.[3]

Ketoses — FRUCTOSE,[1] Sorbose,[2] Tagatose.[3]

Heptoses ($C_7H_{14}O_7$).

Aldose — Mannoheptose.[1]

Ketose — Sedoheptose.[1]

NOTE. — No attempt is here made to summarize the occurrence of any but the tetroses, pentoses, hexoses and heptoses. Glycolose and the trioses if formed in nature are probably too reactive to accumulate sufficiently for identification.

DISACCHARIDES (Disaccharoses).

Dihexoses (Hexobioses) — ($C_{12}H_{22}O_{11}$).

Anhydride of glucose + fructose — SUCROSE.

Anhydrides of glucose + galactose — LACTOSE, Melibiose.

Anhydrides of glucose + glucose — MALTOSE, Isomaltose, Trehalose, Turanose.

TRISACCHARIDES (Trisaccharoses).

Trihexoses ($C_{18}H_{32}O_{16}$).

Anhydride of glucose + galactose + fructose — Raffinose.

Anhydride of glucose + glucose + glucose — Melezitose.

Anhydride of fructose + fructose + fructose — Secalose.

TETRASACCHARIDES (Tetrasaccharoses).

Tetrahexoses ($C_{24}H_{42}O_{21}$).

Anhydrides of 2 galactose + glucose + fructose — Stachyose, Lupeose.

POLYSACCHARIDES (Polysaccharoses).

Pentosans (chief constituents of gums and mucilages).

Anhydrides of xylose — Xylans.

Anhydrides of arabinose — Arabans.

Hexosans.

Anhydrides of glucose — STARCH, CELLULOSE, GLYCOGEN, DEXTRIN (and other "dextrans").

Anhydrides of mannose — Mannans.

Anhydrides of galactose — Galactans (pectins).

Anhydrides of fructose — Inulin (and other "levulans").

---

[1] Occurs free in nature.

[2] Not yet found free in nature (or only in small amounts) but obtained by hydrolysis or fermentation of natural product.

[3] Known only (with certainty) as a laboratory product.

PROPERTIES OF THE CHIEF CARBOHYDRATES OF FOOD

Monosaccharides

The monosaccharides are all soluble, crystallizable, diffusible substances, unaffected by digestive enzymes, and if not attacked by bacteria in the digestive tract, they are absorbed and enter the blood current unchanged. All of the three hexoses described below are susceptible to alcoholic fermentation, and are utilized for the production of glycogen in the animal body and the maintenance of the normal glucose content of the blood. A few of the leading facts regarding the occurrence in food and the nutritive relations of individual monosaccharides are given below.

Glucose (*d.*glucose, dextrose, grape sugar, starch sugar, diabetic sugar) is widely distributed in nature, occurring in the blood of all animals in small quantity (usually about 0.1 per cent) and more abundantly in fruits and plant juices, where it is usually associated with fructose and sucrose. It is especially abundant in grapes, of which it often constitutes 20 per cent or more of the weight of the fresh fruit and considerably more than half of the solid matter. Sweet corn, onions, and unripe potatoes are among the common vegetables containing considerable amounts of glucose.

Glucose is also obtained from many other carbohydrates by hydrolysis either by acids or by enzymes, and thus becomes the principal form in which the carbohydrate of the food enters into the animal economy. In the healthy animal body the glucose of the blood is constantly being burned and replaced. In diabetes the body loses to a greater or less degree the power to burn glucose, which then accumulates in excessive amount in the blood, from which it escapes through the kidneys. A temporary and usually unimportant loss of glucose in the urine may occur as the result of feeding large quantities at a time. This condition is known as alimentary glycosuria. Ordinarily any surplus of glucose absorbed from the digestive tract is converted into glycogen which, as described beyond, is readily reconvertible into glucose. Thus, while other carbohydrates occur in food in greater quantity, glucose occupies a very prominent place, partly because it is more widely distributed than any other carbohydrate, being a normal constituent of both plants and animals, and partly because it is the form in which most of the carbohydrate material of the food comes ultimately into the service of the body tissues (Chapter V). It is estimated that over half the energy manifested in the human body is derived from the oxidation of glucose.

It is not to be inferred from the foregoing statement that the body obtains the energy of the glucose by oxidizing it directly as such. The aldehydic properties of glucose make it susceptible to direct oxidation; but, as the elaborate researches of Nef have shown, the glucose molecule in alkaline solution breaks up to form simpler substances of 2, 3, and 4 carbon atoms which are more readily oxidizable than glucose itself. There is strong evidence (Chapter V) that in the body tissues glucose is broken into 3-carbon molecules, which latter readily undergo oxidation.

Fructose (*d*.fructose, fruit sugar, levulose) occurs with more or less glucose in plant juices, in fruits, and especially in honey, of which it constitutes about one half the solid matter. It results in equal quantity with glucose from the hydrolysis of cane sugar and in smaller proportion from some other less common sugars. Fructose may occur in normal blood, but probably only in insignificant amounts. It serves, like glucose, for the production of glycogen; and the fructose which enters the body either through being eaten as such or as the result of the digestion of cane sugar is mainly changed to glycogen on reaching the liver, so that it does not enter largely into the blood of the general circulation. Glucose and fructose are partially convertible, either one into the other, under the influence of very dilute alkalies. It is not surprising, therefore, that fructose should be converted in the liver into glycogen, which on hydrolysis yields glucose.

Galactose is not found free in nature, but results from the hydrolysis of milk sugar, either by acids or by digestive enzymes, and appears to have the same power as glucose and fructose to promote the formation of glycogen in the animal body. Anhydrides of galactose, known as galactans, occur quite widely distributed in plants; and galactosides, which are compounds containing galactose in chemical combination with radicles of other than carbohydrate nature, are found in the animal body, notably as constituents of the brain and nerve tissues.

Disaccharides

The three disaccharides here considered are di-hexoses or hexo-bioses of the formula $C_{12}H_{22}O_{11}$, and are crystallizable and diffusible. Sucrose crystallizes anhydrous; maltose and lactose, each with one molecule of water, which can be removed by drying at temperatures of 100° and 130° respectively. They are soluble in water; less soluble in alcohol. Lactose is much less soluble than sucrose and maltose. These disaccharides are important constituents of food and are changed to monosaccharides during the process of digestion.

Sucrose (saccharose, cane sugar) is widely distributed in the vegetable kingdom, being found in considerable quantity, generally mixed with glucose and fructose, in the fruits and juices of many plants. The commercially important sources of sucrose are the sugar beet, the sugar and sorghum canes, the sugar palm, and the sugar maple; but many of the common fruits and vegetables contain notable amounts. For example, sucrose is said to constitute at least half the solid matter of pineapples and of some roots such as carrots.

On hydrolysis each molecule of sucrose yields one molecule each of glucose and fructose. These sugars all rotate the plane of vibration of polarized light, sucrose and glucose to the right (+), and fructose to the left (−). The terms "dextrose" and "levulose," synonyms for glucose and fructose respectively, arose from this behavior of the sugars in rotating the plane of polarized light to the right and left. Since at ordinary temperatures the fructose rotates more strongly to the left than the glucose does to the right, the result of the hydrolysis of sucrose is to change the sign of rotation from + to −. For this reason the hydrolysis of cane sugar is often called "inversion," and the resulting mixture of equal parts glucose and fructose is known as "invert sugar."

Sucrose is very easily hydrolyzed either by acid or by the sucrase ("invertase" or "inverting" enzyme) of yeast or of intestinal juice. So far as known neither the saliva nor the gastric juice contains any enzyme capable of hydrolyzing cane sugar, and the slight amount of hydrolysis which takes place in the stomach is believed to be due simply to the presence of hydrochloric acid. Under normal conditions the sucrose of the food passes mainly into the intestine unchanged and is there split by the sucrase of the intestinal juice, and the resulting glucose and fructose are absorbed into the portal blood.

When large amounts of sucrose are fed, some absorption takes place in the stomach; but the unchanged sucrose thus absorbed appears to be largely, if not wholly, lost through the kidneys, as it is when injected directly into the blood current. Sugar eaten in concentrated form or in considerable quantities at a time is apt to cause irritation of the stomach either directly, or as the result of undergoing an acid fermentation, or in both of these ways. According to Herter sucrose and glucose are more likely to ferment in the stomach than is lactose. In cases where fermentation does not occur and the sucrose itself has no irritating effect, it may be especially useful as a rapidly available foodstuff. However, it is not known that sucrose has any advantage over maltose and lactose in this respect, and the latter are less apt to irritate the stomach and cause indigestion.

Lactose (milk sugar) occurs in the milk of all mammals, constituting usually from 6 to 7 per cent of the fresh secretion in human milk and 4.5 to 5 per cent in the milk of cows and goats. At the time of parturition, or if the milk is not withdrawn from the udder, some lactose may occur in the urine. If in such a case the mammary glands are removed, the percentage of glucose in the blood increases, and glucose (but no lactose) may appear in the urine (Abderhalden). These observations indicate that lactose is formed in the mammary gland and probably from the glucose brought by the blood.

Lactose is less sweet and much less soluble than sucrose, dissolving only to the extent of about 1 part in 6 parts of water.

When hydrolyzed either by heating with acids or by an enzyme, such as emulsin or the lactase of the intestinal juice, each molecule of lactose yields one molecule of glucose and one of galactose. In normal digestion, probably none of the lactose eaten is absorbed as such, for lactose injected into the blood is eliminated quickly and almost completely through the kidneys, whereas large amounts of lactose can be taken by the mouth without any such loss. As already noted, Herter found lactose to be less subject to fermentation in the stomach than is sucrose. Also, because of the much lower solubility, there is less danger of direct irritation of the stomach membrane by lactose than by sucrose. Recently Mathews has suggested that the occurrence in milk of lactose, a sugar having the galactose radicle, may be of special significance as a source of material for the synthesis of the galactosides of the brain and nerve tissues of the rapidly growing young mammal.

Maltose (malt sugar) is formed from starch by the action of diastatic enzymes (amylases) and is therefore an important constituent of germinating cereals, malt, and malt products. It is also formed as an intermediate product when starch is hydrolyzed by boiling with dilute mineral acids, as in the manufacture of commercial glucose.

In animal digestion maltose is formed by the action of the ptyalin of the saliva or the amylopsin of the pancreatic juice upon starch or dextrin. The maltose-splitting enzyme of the intestinal juice readily hydrolyzes maltose to glucose. Maltose is also readily and completely hydrolyzed by boiling with dilute mineral acids. In either case each molecule of maltose yields two molecules of glucose.

While it is probable that little if any maltose is absorbed as such from the digestive tract under ordinary conditions, it is possible that such absorption may occur and that maltose as such may play a part in the normal carbohydrate metabolism; for when injected into the blood it appears to be utilized to better advantage than either sucrose or lactose, and it may be obtained from glycogen by the action of diastatic enzymes in much the same way as from starch and dextrin.

Polysaccharides

The polysaccharides are all colloids insoluble in alcohol. Some " dissolve " in water in the sense that they form colloidal dispersions which will pass through filter paper; some swell and become gelatinous; some are unchanged. The members of greatest importance in nutrition are starch and glycogen, the typical reserve carbohydrates of plants and animals respectively.

Pentosans, $(C_5H_8O_4)_x$, occur in the greatest variety of plants and in various parts of the plant organism. As a rule, however, they are abundant only in the fibrous tissues and gummy exudations and not in the starchy and succulent parts which are more commonly used for human food. Moreover experiments have not yet succeeded in demonstrating in man or other mammals any enzyme capable of digesting the pentosans (Swartz). It is therefore believed that, notwithstanding their wide distribution in plants, the pentosans can play only a very small, if appreciable, part in the nutrition of man.

Starch, $(C_6H_{10}O_5)_x$, is the form in which most plants store the greatest part of their carbohydrates, and is of great importance as a constituent of many food materials and as the source of dextrin, maltose, commercial glucose, and many fermentation products. Starch is found stored in the seeds, roots, tubers, bulbs, and sometimes in the stems and leaves of plants. It constitutes one half to three fourths of the solid matter of the ordinary cereal grains and at least three fourths of the solids of mature potatoes.

Unripe apples and bananas contain much starch which is to a large extent changed into sugars as these fruits ripen, while, on the other hand, young tender corn (maize) kernels and peas contain sugar which is transformed into starch as these seeds mature.

Unchanged starch occurs in distinct granules, and those formed in different plants vary in size and structure,* so that in most cases the source of a starch which has not been altered by heat, reagents, or ferments can be determined by microscopical examination. Starch granules are scarcely affected by cold water; on warming they absorb water and swell. Finally the starch passes into a condition of colloidal dispersion or semi-solution, "starch paste." Starch which has been heated in water (either admixed or naturally present with the starch as in a potato) until the granules are ruptured and the material more or less dispersed is very much more rapidly hydrolyzed by digestive ferments than is raw starch.

To colloids such as starch, the usual methods of determining molecular weight are not applicable. It is certain, however, from the chemical complexity of some of the dextrins which result from hydrolysis of starch, that the molecular weight of starch must be very high and its chemical constitution very complex. Probably the value of x in the formula $(C_6H_{10}O_5)_x$ is very large, perhaps in the neighborhood of 200, corresponding to a molecular weight of about 32,000. For a full discussion of the more important facts bearing on the chemical constitution of starch, see the paper by Thomas cited in the list of references at the end of the chapter.

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* A very detailed study of the starch granules of different species of plants has been made by Reichert and published by the Carnegie Institution of Washington. (See references at end of chapter.)

Starch either in the solid or in the "soluble" (dispersed) form is colored intensely blue when treated with iodine. This well-known reaction is delicate and distinctive, but is now believed to be due to colloidal adsorption rather than to the formation of a definite chemical compound.

The term "starch," as we ordinarily use it, probably covers at least two substances. The more abundant of these, α-amylose (also called "amylopectin"), forms on heating in water a viscous opalescent paste, gives a somewhat purplish blue color with iodine, is evidently of great molecular complexity, and has recently been found to contain a small amount of phosphorus * as an essential constituent. The less abundant component of starch, β-amylose (also called "amylose"), forms when heated in water a clear, limpid solution which gives a pure blue color with iodine. The starch-digesting enzymes hydrolyze both α-amylose and β-amylose, but not always with equal facility.†

Starch on hydrolysis by means of acid gives first mixtures of dextrin and maltose, and finally glucose only as an end-product. The most satisfactory hydrolysis of starch to glucose is accomplished by boiling or heating in a boiling water bath with hydrochloric acid of a concentration of about 2.5 per cent. When brought in contact with saliva, starch is hydrolyzed by

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* In the case of potato starch about 0.06 per cent. See papers by Northrup and Nelson and by Thomas referred to at the end of the chapter.

† See paper by Sherman and Baker referred to at the end of the chapter.

the ptyalin, with the formation of dextrin and maltose. A similar hydrolysis is affected by "amylopsin," the starch-splitting enzyme of the pancreatic juice, preferably known as pancreatic amylase (see terminology of enzymes, Chapter IV).

"Soluble starch," largely used for laboratory experiments, is usually prepared by soaking raw starch in cold hydrochloric acid (about 7 per cent HCl) for several days, and then washing with cold water.

Dextrins, $(C_6H_{10}O_5)_x$ or $(C_6H_{10}O_5)_x \cdot H_2O$, are formed from starch by the action of enzymes, acids, or heat. Small amounts of dextrin are found in normal, and larger amounts in germinating, cereals. Malt diastase, acting for some time upon starch in fairly concentrated solution, yields usually about one part of dextrin to four of maltose. During acid hydrolysis, dextrin is formed as an intermediate product between soluble starch and maltose. Commercial dextrin, the principal constituent of "British gum," is obtained by heating starch, either alone or with a small amount of dilute acid.

The dextrins are much more soluble than the starches; and dextrin molecules while doubtless very large and complex are probably not over one fifth the size of starch molecules.

The digestion of dextrin has already been mentioned in connection with that of starch, both saliva and pancreatic juice forming dextrin during the digestion of starch and acting upon it with the production of maltose. Complete hydrolysis of dextrin, as by boiling with acid, yields glucose as the sole product.

Glycogen, $(C_6H_{10}O_5)_x$, plays much the same rôle in animals which starch plays in plants, and is sometimes called "animal starch." Glycogen also takes the place of starch as reserve carbohydrate in fungi and other forms of plant life not provided with the chlorophyll apparatus. It is a white, amorphous powder, odorless and tasteless, which swells up and apparently dissolves in cold water to an opalescent colloidal dispersion which is not cleared by repeated filtration, but loses its opalescence on addition of a very small amount of potassium hydroxide or acetic acid. Water solutions (dispersions) of glycogen are readily precipitated by alcohol. When treated with iodine they react yellow-brown, red-brown, or deep red. Hydrolysis of glycogen yields glucose only, as end-product.

Glycogen occurs in the lower as well as the higher animals, and in all parts of the body, but is especially abundant in the liver. The amount of glycogen in the liver depends to a great extent upon the condition of nutrition of the animal. In the average of seven experiments by Schöndorff in which dogs were fed for the production of as much glycogen as possible, 38 per cent of that found was in the liver, 44 per cent in the muscles, 9 per cent in the bones, and the remaining 9 per cent in the other tissues of the body. But the distribution of glycogen in the body as shown by these experiments was quite variable, even among animals of the same species which had been fed in the same way. It is well known, too, that some species store glycogen in their muscles to a greater extent than others, attempts even having been made to distinguish analytically between horseflesh and beef by the difference in their glycogen content. The storage of glycogen in the body is promoted by rest as well as by liberal feeding, and stored glycogen is used up rapidly during active muscular work.

Cellulose, $(C_6H_{10}O_5)_x$, the chief constituent of wood and of the walls of plant cells generally, is an anhydride of glucose and can be made to yield the latter when hydrolyzed by suitable treatment with strong acid. Typical cellulose of mature fiber (such as cotton, linen, or wood fiber) is, however, quite resistant to the action of dilute acids or of ordinary enzymes and passes through the digestive tract for the most part unchanged. The toughness of the cellulose differs with the stage of growth or maturity, and some of the less resistant forms of cellulose, such as that of tender white cabbage, may disappear from the digestive tract in appreciable amounts. Experiments to determine whether the cellulose thus disappearing is digested to sugar and absorbed or merely decomposed by bacteria in the digestive tract have not given conclusive results. According to Swartz: "In any event, the quantities of cellulose which the alimentary tract of man is capable of absorbing are, apparently, too small for it to play a rôle of any importance in the diet of a normal individual." The cellulose in the food may, however, serve a very useful purpose in giving bulk to the food residues and thus facilitating their passage along the digestive tract.

Hemicelluloses is a term somewhat loosely applied to polysaccharides, usually occurring as constituents of cell walls in plants, which are not digested by the starch-splitting enzymes but are usually much more readily hydrolyzed by acid than is cellulose. In many plant tissues the hemicellulose consists chiefly of pentosans; in other cases it is largely mannan or galactan.

Mannans, $(C_6H_{10}O_5)_x$, anhydrides of mannose, are widely distributed in the vegetable kingdom and, as Swartz points out, show great differences in solubility, ranging from the readily soluble mucilaginous forms found in certain legumes to the horny matter of such seeds as the date, a form of mannan which was long confused with true cellulose. The experiments of Swartz upon the mannan of salep showed it to disappear completely in its passage through the human digestive tract, although tests with individual digestive enzymes gave negative results. In what way and to what extent the mannan thus disappearing from the digestive tract becomes available in nutrition is still a subject of investigation.

Galactans, $(C_6H_{10}O_5)_x$, anhydrides of galactose, are widely distributed in plants. They occur in the seeds of legumes and to a slight extent in the cereals also, in by-products of beet sugar manufacture and abundantly in several of the algæ and lichens, including Chinese moss, agar-agar, and Irish moss. The pectins are said to consist largely of galactans, apparently either in combination or admixture with pentosans and perhaps other complexes as well. The galactans differ in their solubilities and apparent digestibility when eaten by man or other animals, but on the whole do not appear to be of much nutritive value. Those of agar-agar and Irish moss, which are most used as food, are not digested.

Levulans is the term under which a number of polysaccharides of the composition $(C_6H_{10}O_5)_x$, and yielding fructose (levulose) on hydrolysis have been described. The most important of these, at least so far as is at present known, is *inulin*, a white, powdery substance occurring in the tubers of the Jerusalem artichoke and to a less extent in the bulbs of onions and garlic as well as in various parts of plants not commonly used for food. By the action of acids inulin is very readily hydrolyzed to levulose, but the digestive juices do not seem to contain enzymes capable of hydrolyzing inulin and it appears to be of practically no importance as human food.

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CHAPTER II

FATS AND LIPOIDS

Almost as widely distributed in nature as the carbohydrates, and constituting a much more concentrated form of fuel to supply energy in nutrition, are the fats. Fats are glyceryl esters of fatty acids, and since glycerol is a triatomic alcohol and the fatty acids are monatomic, a normal glyceride is a triglyceride and on hydrolysis yields three molecules of fatty acid and one molecule of glycerol. Thus, for example:

$$\underset{\substack{\text{Stearin}\\\text{(glyceryl tristearate)}}}{C_3H_5(C_{18}H_{35}O_2)_3} + 3\,H_2O \rightarrow \underset{\text{Glycerol}}{C_3H_5(OH)_3} + 3\,\underset{\text{Stearic acid}}{C_{18}H_{36}O_2}.$$

When the splitting of the fat is brought about by means of an alkali instead of water, the corresponding products are glycerol and three molecules of the alkali salt of the fatty acid. Since alkali salts of the fatty acids are commonly known as soaps, this reaction is usually called saponification of the fat.

The fats are therefore a definite group of chemical compounds, and the term applies equally to the solid and the liquid members of this group. As a matter of convenience, however, the liquid fats are often called "fatty oils." The fatty oils are also sometimes called "fixed oils," since a spot made by dropping a fatty oil on paper cannot be removed by drying (as can a volatile oil), nor by washing with water (as can glycerin).

Another property which helps to characterize the fats is that glycerol, or the glyceryl radicle of a fat, when heated to a high temperature (300° C. or over), decomposes with production of acrolein, an aldehyde of characteristic odor and very irritating to the mucous membranes. Doubtless also fatty acid radicles may sometimes contribute to the production of irritating fumes when fat is overheated.

The fats, including fatty oils, are lighter than water, their specific gravities ranging between 0.90 and 0.97. They are poor conductors of heat and therefore tend to conserve the heat of the body, while they show on oxidation a much higher fuel value than any of the other foodstuffs.

All of the fats are practically insoluble in water, and all except those of the castor oil group are sparingly soluble in cold alcohol, but dissolve readily in petroleum ether and mix in all proportions with light petroleum oils. Light petroleum distillate (" petroleum ether ") is often used as a solvent for fat. All of the fats are readily soluble in ether, carbon bisulphide, chloroform, carbon tetrachloride, and benzene. Since neither carbohydrates, proteins, nor ash constituents are soluble in ether (or the other " fat solvents "), it follows that the fat of a food may be readily separated from the other chief components by drying the food and extracting the dry material with pure ether. After the fat has been completely dissolved away from the other foodstuffs, it can be recovered from the solvent by evaporating the latter at a relatively low temperature. This is the method commonly used to estimate the percentages of fat in foods and to obtain small portions of fat for examination. It must be noted, however, that the fat thus obtained is not always pure in the sense of consisting entirely of substances meeting the definition of fat as given above. Obviously, such an extract will contain, along with the fat, any other ether-soluble substances which were present in the food, and may contain substances which, while not appreciably soluble in ether alone, are dissolved by the mixture of ether and fat. It is therefore somewhat more accurate to speak of the material extracted by ether as " ether extract " rather than as " fat," and it will be found so designated in some statements of analytical results. In most human foods — at least those which are important as sources of fat — the constituents of the ether extract other than true fat are for the most part fat-like substances and we shall therefore be sufficiently accurate in most cases if we designate the material extracted by ether by the simple term " fat," remembering, however, that we may thus include along with the glycerides (and any free fatty acids which may be present) small amounts of *fat-like* substances or *lipoids*, and of fat-soluble or other ether-soluble matter.

The food fats of commerce have been separated from the materials in which they naturally occurred not by solvents as above described but by mechanical means such as churning (butter) or pressing (olive or cottonseed oil) but even in this case the naturally occurring fat-soluble substances will still remain dissolved in the separated fat. Recent investigations indicate that these fat-like and fat-soluble substances, although occurring only in small quantities, may have very important functions in nutrition. We shall have occasion to study them in that connection later.

The actual glycerides of any common natural fat, with the exception of butter, would if obtained absolutely pure be colorless, tasteless, and odorless. The colors, tastes, and odors of fats are therefore ordinarily due to substances present in small amount which might be removed by refining processes. All of the quantitative differences among the fats are to be accounted for by the kinds and the amounts of the fatty acids which enter into the composition of the glycerides.

Fatty Acids

The greater number of the fatty acids belong to a few homologous series. The series to which stearic acid belongs may be represented by the general formula, $C_nH_{2n}O_2$, and is made up of homologues of acetic acid. The principal members of physiological importance are as follows:

ACIDS OF THE SERIES $C_nH_{2n}O_2$

Butyric acid ($C_4H_8O_2$) occurs as glyceride to the extent of about 5 to 6 per cent in butter and in very small quantities in a few other fats.

Caproic acid ($C_6H_{12}O_2$) is obtained from goat and cow butter and coconut fat.

Caprylic acid ($C_8H_{16}O_2$) is obtained from coconut oil, butter, and human fat.

Capric acid ($C_{10}H_{20}O_2$) is obtained from coconut oil, butter, and the fat of the spice bush.

Lauric acid ($C_{12}H_{24}O_2$) occurs abundantly as glyceride in the fat of the seeds of the spice bush, and in smaller proportions in butter, coconut fat, palm oil, and some other vegetable oils.

Myristic acid ($C_{14}H_{28}O_2$) is obtained from nutmeg butter, coconut oil, butter, lard, and many other fats, as well as from spermaceti and wool wax.

Palmitic acid ($C_{16}H_{32}O_2$) occurs abundantly in a great variety of fats, both animal and vegetable, including many fatty oils, and also in several waxes, including spermaceti and beeswax.

Stearic acid ($C_{18}H_{36}O_2$) is found in most fats, occurring more abundantly in the solid fats and especially in those having high melting points.

Butyric acid is a mobile liquid, mixing in all proportions with water, alcohol, and ether, boiling without decomposition, and readily volatile with steam. With increasing molecular weight the acids of this series regularly show increasing boiling or melting points, decreasing solubility, and loss of volatility with steam. For ordinary temperatures the dividing line between liquids and solids falls at about capric acid. Stearic acid is a crystalline solid, insoluble in water, and only moderately soluble in alcohol and ether.

ACIDS OF THE SERIES $C_nH_{2n-2}O_2$

These are unsaturated compounds. Each molecule contains one ethylene linkage or "double bond," and can take up by addition two atoms of halogen to form a saturated compound.* These unsaturated acids have, as a rule, much lower melting points than the saturated acids containing the same number of carbon atoms. The glycerides show correspondingly lower melting points than those of the saturated fatty acids and are therefore found more largely in the soft fats and the fatty oils. Such soft fats or fatty oils can be hardened to any desired consistency (up to that of stearin) by hydrogenation, which changes the unsaturated fatty acid radicles into the corresponding members of the saturated series. In recent years this process has been exploited commercially and large quantities of refined cottonseed oil are now hydrogenated to the consistency of lard and sold under trade names as lard substitutes. Other oils are also hardened by hydrogenation.

Phycetoleic acid ($C_{16}H_{30}O_2$) is obtained from seal oil and sperm oil; an isomeric acid, *hypogæic*, occurs in peanut oil.

Oleic acid ($C_{18}H_{34}O_2$) occurs as glyceride in nearly all fats and fatty oils and is much the most important member of the series. Many of the typical oils of both animal and vegetable origin, such as lard oil and olive oil, consist mainly of olein.

Erucic acid ($C_{22}H_{42}O_2$) is obtained from rape seed and mustard seed oils, and is not found in animal fats except when oils which contain this acid have been fed to the animal.

The gradual change in physical properties with increasing molecular weight which is noticeable in the stearic acid series is not apparent in this series, probably because the known acids of the series differ as regards the position of the double bond and are therefore not strictly homologous.

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* The relative number of double bonds is measured analytically by determining the percentage of iodine which the fat or fatty acid will absorb. Thus pure oleic acid (mol. wt. 282) absorbs 2 atoms of iodine, giving an "iodine number" of 90; pure linoleic acid would absorb 4 atoms of iodine to the molecule, giving an "iodine number" about twice as great.

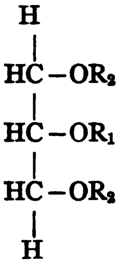
OTHER UNSATURATED FATTY ACIDS

Acids of the series $C_nH_{2n-4}O_2$, $C_nH_{2n-6}O_2$, and $C_nH_{2n-8}O_2$ have been found to occur as glycerides in some of the fats. *Linoleic acid*, $C_{18}H_{32}O_2$, and *linolenic acid*, $C_{18}H_{30}O_2$, are the best known of these acids. They are found abundantly in linseed oil and in others of the so-called "drying oils," which on account of the affinity for oxygen of their highly unsaturated glycerides are gradually oxidized to solids on exposure to the air. Fatty acids having the same number of double bonds, but not the same property of oxidizing to hard, solid films are found in fatty oils of animal origin, especially those obtained from marine animals and from fishes. Since the acids of this series have still lower melting points than the corresponding acids of the oleic series, and since the physical properties of the glycerides follow those of the fatty acids which they contain, a fat containing an acid isomeric with linoleic or linolenic acid will be more fluid at any given temperature than one containing oleic acid in the same proportion. Hence, it is apparent that glycerides of the highly unsaturated and more fluid acids are physiologically adapted to the cold-blooded animals, and it is found that they are especially abundant in fish fat; the acids of the series $C_nH_{2n-8}O_2$ have been obtained as yet only from fish oils.

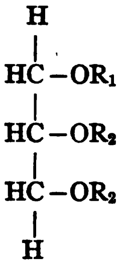
"Simple" and "Mixed" Triglycerides

Triglycerides in which the three fatty acid radicles are of the same kind are known as *simple triglycerides*. Tristearin, triolein, tripalmitin, etc., are examples of simple triglycerides. A *mixed triglyceride* is one in which the three fatty acid radicles are not all of the same kind. For example, distearo-olein (having two radicles of stearic and one of oleic acid), dioleo-palmitin (having two of oleic and one of palmitic), or stearo-oleo-palmitin (having one radicle each of stearic, oleic, and palmitic acids), is each a mixed triglyceride.

It is evident from the chemical structure of glycerol that there can be only one simple triglyceride of any given fatty acid but that with two fatty acid radicles alike (R_2) and one different (R_1) the triglyceride may have either of the following forms:



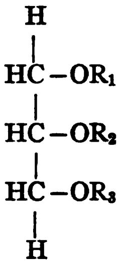
$$\begin{array}{l}\;\;\mathrm{H}\\\;\;|\\\mathrm{HC-OR_2}\\\;\;|\\\mathrm{HC-OR_1}\\\;\;|\\\mathrm{HC-OR_2}\\\;\;|\\\;\;\mathrm{H}\end{array}$$



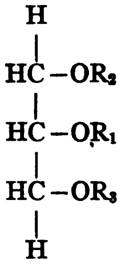
$$\begin{array}{l}\;\;\mathrm{H}\\\;\;|\\\mathrm{HC-OR_1}\\\;\;|\\\mathrm{HC-OR_2}\\\;\;|\\\mathrm{HC-OR_2}\\\;\;|\\\;\;\mathrm{H}\end{array}$$

That is, the two radicles of the same kind may be on the terminal carbons or may be adjacent. It will be noted that the two substances here represented have exactly the same composition, but different constitution.

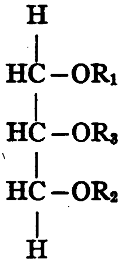
If now the triglyceride contains one each of three different acid radicles (R_1, R_2, R_3) there are plainly three possible forms:



$$\begin{array}{l}\;\;\mathrm{H}\\\;\;|\\\mathrm{HC-OR_1}\\\;\;|\\\mathrm{HC-OR_2}\\\;\;|\\\mathrm{HC-OR_3}\\\;\;|\\\;\;\mathrm{H}\end{array}$$



$$\begin{array}{l}\;\;\mathrm{H}\\\;\;|\\\mathrm{HC-OR_2}\\\;\;|\\\mathrm{HC-OR_1}\\\;\;|\\\mathrm{HC-OR_3}\\\;\;|\\\;\;\mathrm{H}\end{array}$$



$$\begin{array}{l}\;\;\mathrm{H}\\\;\;|\\\mathrm{HC-OR_1}\\\;\;|\\\mathrm{HC-OR_3}\\\;\;|\\\mathrm{HC-OR_2}\\\;\;|\\\;\;\mathrm{H}\end{array}$$

Each of these three substances has exactly the same composition, though the constitution is different for each.

It should be noted that these five formulæ represent types of structure and that the actual number of triglycerides possible from three fatty acid radicles is greater since we may have substances corresponding to either of the first two in which R_3 replaces either R_1 or R_2; and it is plain that as the number of fatty acids is increased beyond three the number of possible mixed triglycerides increases very rapidly so that with the large number of fatty acids which are now known to be of fairly common occurrence in fats the possible number of mixed triglycerides must be almost unlimited. The simple triglycerides corresponding to the common fatty acids are all known, but naturally not all of the practically innumerable possible mixed triglycerides have been separated or prepared.

Berthelot in 1869 suggested that fats probably contain mixed glycerides and in 1889 Blyth and Robertson reported a palmito-stearo-olein in butter, but it is only since Kreis and Hafner (1903) described the preparation of *palmito-distearin* from beef tallow and Bömer (1909) separated *stearo-dipalmitin* from mutton tallow and *palmito-distearin* from lard that the widespread occurrence of mixed glycerides in the familiar fats has been generally accepted.

Among the other mixed glycerides reported as having been isolated from natural fats are:

Myristo-palmito-olein in cacao butter (Klimont, 1902), *dipalmito-olein* and *stearo-palmito-olein* in tallow (Hansen, 1902), *distearo-olein* in cacao butter (Fritzweiler, 1903) and in Borneo tallow (Klimont, 1905), *stearo-diolein* in human fat (Partheil and Ferie, 1903).

The fact long known to analysts that fats too nearly identical in composition to be distinguished by chemical analysis may still show differences in crystalline structure under the microscope is now explained as due to the presence of different mixed triglycerides containing the same fatty acid radicles. Thus beef fat rendered at such a temperature as to contain the glycerides of stearic, palmitic, and oleic acids in practically the same proportions as in lard still differs so constantly from lard in its microscopic appearance as to indicate the presence of distinct chemical substances and has now been shown to contain different mixed triglycerides.

The fact that tributyrin has an intensely bitter taste makes it seem probable that none of this substance occurs in butter but rather that the butyric acid in butter fat is in the form of mixed glycerides. Probably mixed glycerides are as abundant as simple glycerides in natural fats.

Formation and Composition of Natural Fats

Fats are formed both in plants and in animals. The conditions which determine fat formation, and the character of the fat formed in different species and under different conditions, are better known than the chemical steps involved in the process. It is hardly necessary to mention the fact that the true fats are composed of the same three chemical elements of which the carbohydrates are composed (carbon, hydrogen, and oxygen) and that since the fats contain less oxygen and more carbon and hydrogen than the carbohydrates, they constitute a more concentrated form of fuel or a more compact and lighter medium for the storage of energy for future use. The question therefore presents itself whether either the plant or the animal organism (or both) has the power to change carbohydrate material into fat.

Formation of Fat from Carbohydrate

In plants there are many indications of the formation of fat from carbohydrate, as when decrease of starch and increase of fat go on simultaneously in a ripening seed, or when sugars are found to be constantly brought to a tissue in which fat is forming and there disappear as the formation of fat progresses. It is probably because no one has doubted the formation of fat from carbohydrate in plants that the process has not been more rigorously investigated.

In animals it is certain that fat may be formed from carbohydrate. From the standpoint of our present knowledge it would seem that the readiness with which farm animals are fattened on essentially carbohydrate food should have been sufficient to convince early observers; but this evidence appears to have been overlooked formerly because of the idea, for a long time prevalent, that simpler substances are built up into more complex compounds only in the plant, and not in the animal organism. In recent years it has become necessary to abandon this latter assumption completely, and there is now abundant evidence that the animal body synthesizes fat from carbohydrate.

The most obvious method of demonstrating the conversion of carbohydrate into fat is that followed by Lawes and Gilbert. Several pigs of the same litter and of similar size were selected; some were killed and analyzed as "controls," while the others were fed on known rations and later weighed, killed, and analyzed to determine the kinds and amounts of material stored in the body. In several cases the amounts of fat stored during such feeding trials were found to have been much larger than could be accounted for by all of the fat and protein fed, so that at least a part, and in some cases the greater part, of the body fat must have been formed from the carbohydrate of the food. Many similar experiments have been made, and the transformation of carbohydrate into fat has been demonstrated by this method in carnivorous as well as herbivorous animals.

It has also been shown that carbohydrates contribute to the production of milk fat. Jordan and Jenter kept a milch cow for fifty-nine days upon food from which nearly all of the fat had been extracted. During this period about twice as much milk fat was produced as could be accounted for by the total fat and protein of the food, and in addition the cow gained in weight and her appearance showed that she had more body fat at the end than at the beginning of the experiment.

Instead of determining directly the fat formed in the animal fed on carbohydrate, the production of fat from carbohydrate may be demonstrated by keeping the animal experimented upon in a respiration chamber so arranged that the total carbon given off from the body may be determined and compared with the total carbon of the food. If in such a case the body is found to store more carbon than it could store as carbohydrate or protein, it is safe to infer that at least the excess of stored carbon is held in the form of fat. Many such experiments upon dogs, geese, and swine have shown storage of carbon very much greater than could be accounted for on any other assumption than that a part of the carbon of the carbohydrates eaten remained in the body in the form of fat.

Further evidence of the transformation of carbohydrate into fat in the animal body is obtained from the "respiratory quotient." The discussion of the quotient and the significance of the information which it furnishes, as also the study of the chemical steps through which the transformation of carbohydrate into fat may take place, will be taken up in connection with the general study of the fate of the foodstuffs in metabolism (Chapter V).

Composition and Properties of Animal Fat

Just as we found that the character of the fat of the cold-blooded animals is adapted to the maintenance of a fluid or plastic consistency at the low temperature to which it is exposed, so to a less degree the character of the fat of warm-blooded animals appears to vary with its position in the body and with the temperature to which the body is subjected during the time that the fat is in process of formation. Thus Henriques and Hansen concluded from experiments with pigs that the thick layer of subcutaneous fat on the back, where it was not thoroughly warmed by the blood and therefore had an average temperature considerably below that of the interior of the body, was richer in unsaturated compounds (olein, etc.) and had a lower melting point than the fat of the body as a whole; while the fat from animals which had been grown in a warm room, or which had been heavily jacketed so that the skin was not exposed to cold air, contained near the skin fat of more nearly the same composition as in the interior of the body.

Moulton and Trowbridge have observed that the fat in beef animals becomes richer in olein and therefore softer with age, with fatness, and with nearness to the surface of the body.

Usually, however, the nature of the fat found in the body is more or less characteristic of each species or group of closely related species. Herbivora contain as a rule harder fats than carnivora, land animals have harder fats than marine animals, and all warm-blooded animals have fats which are decidedly harder than those found in fishes. The fats of different mammals were investigated by Schulze and Reineke, whose results * showed little variation from an average of carbon, 76.5 per cent; hydrogen, 12 per cent; oxygen, 11.5 per cent, as may be seen from the following:

KIND OF FAT	CARBON	HYDROGEN	OXYGEN
Human fat †	76.62	11.94	11.44
Beef fat	76.50	11.91	11.59
Mutton fat	76.61	12.03	11.36
Pork fat	76.54	11.94	11.52

The foregoing statements refer to the fat of the adipose tissues. In the fat extracted from the liver, kidney, and heart,

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* Armsby's *Principles of Animal Nutrition*, page 61.

† Benedict and Osterberg (*American Journal of Physiology*, Vol. 4, page 69) found in 8 samples of human fat an average of 76.08 per cent carbon and 11.78 per cent hydrogen.

Hartley* finds fatty acids of the series $C_nH_{2n-4}O_2$, $C_nH_{2n-6}O_2$, and possibly $C_nH_{2n-8}O_2$.

A possible explanation of this difference between the fat of the adipose tissues and of the actively functioning organs is to be found in the greater reactivity of the unsaturated acid radicles. The saturated fatty acid radicles are relatively stable and inert; and when the glycerides of such acids are deposited in the inactive adipose tissues, the fats may remain unaltered for a long time and accumulate in considerable quantities. The unsaturated fatty acid radicles are less stable and more readily acted upon and broken up. This is consistent with the fact that we find them more abundantly in fats of the organs in which metabolism is more active and has led to the view that the desaturation of fatty acid radicles by the active organs of the body may be an important preliminary to the metabolism of the fat. On the other hand, the formation of unsaturated fatty acid radicles such as oleic and linoleic does not, according to our present knowledge, seem essential to the "β-oxidation theory" which is now generally held as most probably representing the main course of fatty acid metabolism (Chapter V). It is therefore entirely possible that the highly unsaturated fatty acids found, for example, in the liver, may be present as constituents of the protoplasm of these cells, essential to the properties which enable them to carry out some of their functions but not necessarily connected with the metabolism of fat itself.

Butter fat differs from body fat in containing fatty acids of lower molecular weight (particularly butyric acid, which is fairly characteristic of butter), and so shows a higher percentage of oxygen and lower percentages of carbon and hydrogen. The most abundant acids of butter fat are, however, palmitic, oleic, and myristic, and the ultimate composition is not very greatly different from that of body fats. A sample of butter fat analyzed by Browne* showed 75.17 per cent carbon, 11.72 per cent hydrogen, and 13.11 per cent oxygen.

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* *Journal of Physiology*, Vol. 36, page 17.

Storage of Food Fat in the Body

In discussing the formation of body fat from carbohydrate it was shown that often the greater part of the fat stored is manufactured in the body from carbohydrate. So striking were the results of some of the experiments demonstrating the synthesis of fat from carbohydrate, that physiologists came to question for a time whether any of the fat deposited in the tissues comes from the fat of the food. Abundant evidence that food fats may be directly deposited in the body has been obtained by feeding characteristic fats to dogs and showing that these fats can afterwards be recognized in the tissues of the animals. Experiments of this kind have been made, using linseed oil, rapeseed oil, or mutton tallow, any of which is easily distinguishable by its chemical and physical properties from the fat normally found in the body of the dog. For example, Munk starved a dog for 19 days, and then for 14 days fed a mixture of the fatty acids obtained from mutton tallow, as a consequence of which about one half of the weight lost by fasting was regained. The dog was then killed and yielded on dissection 1100 grams of fat melting at 40°, which is about the melting point of mutton tallow, whereas normal dog fat melts at about 20°. In another experiment by Munk rape oil was fed and the fat obtained from the dog was found to contain 82.4 per cent of oleic and erucic acids and 12.3 per cent of solid acids, whereas normal dog fat had only 65.8 per cent oleic, no erucic, and 28.8 per cent of solid fatty acids.

The occurrence in the body fat of properties usually characteristic of some particular fat which has been fed is now very well known and is recognized in establishing standards of purity

* *Journal of the American Chemical Society*, Vol. 21, page 823 (1899).

for fats of animal origin. Thus, the lard obtained from swine which have been fed cottonseed meal shows the characteristic color reactions of cottonseed oil, and more elaborate tests must be made in order to determine whether cottonseed fat has actually been mixed with the lard.

European food officials sought to establish an easy method of distinguishing between butter and its substitutes by requiring manufacturers of any butter substitute to use a certain proportion of sesame oil in the preparation, sesame oil having a characteristic color reaction which can be very easily demonstrated without the use of laboratory facilities. It was found, however, that the same sesame oil reaction might be exhibited by a perfectly pure butter fat from cows which had been fed upon sesame meal.

Evidence of the formation of body fat from food fat has also been obtained by experiments upon the total amount of fat formed in the body when the amount and composition of the food eaten was accurately known. Hoffmann starved a dog until its weight had decreased from 26 to 16 kilograms, so that it must have been almost devoid of fat. He then fed small amounts of meat and large amounts of fat for five days, after which the dog was killed and analyzed. The body contained 1353 grams of fat, of which not over 131 grams could have come from proteins, and only a few grams at most from the small amount of carbohydrates in the meat fed, so that about nine tenths of the fat which the animal had laid on must have come from the fat of the food.

Thus there is abundant experimental evidence that both the carbohydrate and the fat of the food may serve as sources of body fat. In a later chapter it will be shown that protein also may contribute to the production of fat in the body.

A question naturally arises as to how, if proteins, fats, and carbohydrates of food may all contribute to the production of body fat, the nature of the fat can still be to any significant degree characteristic of the species in which it is found. A partial explanation appears to be furnished by the recent work of Bloor, who finds that when the fat of the food has been split to glycerol and fatty acids in the course of digestion and these digestion products are taken up and resynthesized to fat in the intestinal wall, there may go into the resynthesized fat not only the fatty acid radicles of the food fat but also fatty acid radicles formed in the body. These latter, entering into the constitution of the absorbed fat, tend to give it some of the properties characteristic of the species while at the same time some of the characteristics of the food fat may be retained. Thus when a dog is fattened by feeding mutton tallow which contains more stearin and less olein than ordinary dog fat the organism may, if the fattening is gradual, furnish enough oleic acid radicles to bring the resynthesized fat to the consistency ordinarily found in dog fat, or if the fattening is more rapid the oleic acid radicles may not be supplied at a sufficiently rapid rate to yield this result and the dog will then lay on fat of a character somewhere between that of mutton tallow and ordinary dog fat, the influence of the food fat upon the character of the stored fat being more pronounced the more rapidly the fattening is carried out. It will be noted that, even if the fatty acid radicles synthesized in the body are built into the absorbed fat to such an extent as to bring its consistency and other physical properties to what is characteristic for the species, yet such body fat may still contain some radicles of fatty acids characteristic of the experimental food and not ordinarily found in the fat of the animal, as in the case of erucic acid in the experiment cited above (page 32).

Fats and Lipoids as Body Constituents

From what has been stated above, fat is seen to be a form of reserve fuel to which any of the organic foodstuffs may contribute (see also the discussion of fate of the foodstuffs in

Chapter V). It is as reserve fuel that the large deposits of body fat are chiefly significant, but it should not be forgotten that even this " depot fat " may function as a protection to the body from mechanical injury and too rapid a loss of heat when exposed to cold, and as a packing and support to the visceral organs, particularly the kidneys. In recent years it has come to be recognized that modified fats and fat-like substances (lipoids) are essential constituents of body tissues. Thus cell membranes are not simply walls of protein matter but probably are composed of both proteins and lipoids of different kinds and in varying proportions, and protoplasm is to be thought of as an emulsion of proteins and lipoids rather than as a jelly of proteins alone.

Taylor, writing in 1912, says: * " Fat plays two rôles within the body. Fat represents the ultimate form of the storage of fuel, and the depot fats are quite the most inert and dead of any of the body structures. On the other hand, fats joined with protein and in complex combinations of still unknown composition, represent the most essential structures in cellular protoplasm, cell membranes, and in the central nervous system. The subjects of fat in its cellulometabolic relations and fat in the energy metabolism are almost as distinct as though different substances were under consideration. Our information on the two subjects is not equal; we know much concerning fat as fuel; we know little concerning fat in cellular structure."

Mathews, in 1915,† writes: "It will be recalled that all living matter contains a larger or smaller amount of organic substances which are soluble in alcohol, ether, and other fat solvents. These substances help to give to protoplasm its properties of containing large amounts of water but not dissolving; and also the power of taking up readily and in large amounts chloroform, ether, and other substances soluble in fats but not readily soluble in water. They are among the fundamental and ever-present constituents of living matter."

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* *Digestion and Metabolism*, page 342.

† *Physiological Chemistry*, page 61.

Following the suggestion of Gies,* Mathews includes all such substances under the group name of *lipins* (from the Greek, *lipos*, fat) which is thus made to cover both the true fats and all fat-like or lipoid substances. According to Mathews' classification based on that proposed by Gies, the term "lipins" covers: "Alcohol-ether soluble constituents of protoplasm having a greasy feel and insoluble in water." These are divided into nine groups as follows:

1. Fats and fatty acids, the term "fat" being here confined to those neutral glycerides which are solid at 20° C.
2. Fatty oils (liquid at 20°C.) including (1) drying oils such as linseed oil, (2) semidrying oils such as cottonseed oil, (3) non-drying oils such as olive oil.
3. Essential oils. Volatile, generally odoriferous, oil substances of varied chemical nature.
4. Waxes. Esters of fatty acids with monatomic alcohols of high molecular weight such as the sterols.
5. Sterols. Alcohols, generally of terpene group, soluble at ordinary temperatures. Cholesterol, phytosterol, etc.
6. Phospholipins. Phosphatids. Fatty substances, yielding on hydrolysis phosphoric acid and fatty acids (as well as glycerol). Lecithin, cephalin.
7. Glycolipins. Fatty substances free from phosphorus, yielding on hydrolysis fatty acids and a carbohydrate. Cerebron, phrenosin.
8. Sulpholipins. Fatty substances, yielding on hydrolysis fatty acids and sulphuric acid. Sulphatide of brain.
9. Aminolipins. Fatty substances, free from phosphorus, which contain amino nitrogen.

Mathews remarks: "While the group of lipins contains such widely different chemical substances as the aromatic essential oils, like clove oil, the true neutral fats, like mutton tallow, the sterols, which are aromatic alcohols, and the phosphatids, or phospholipins, which contain large amounts of phosphoric acid, the members of the group all possess two or three properties by virtue of which they are called lipins. These properties are their greasy or fat-like feel, their solubility in chloroform and fat solvents, and their insolubility in water. They constitute, then, a very heterogeneous group, chemically and physiologically."

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* A more elaborate classification of the lipins is suggested by Gies and Rosenbloom in the article cited at the end of this chapter.

We have therefore, in the large heterogeneous group of substances called lipins: (1) true fatty substances — fats, fatty oils, fatty acids, (2) fat-like or lipoid substances — some of these latter (like lecithin and other phospholipins) being closely related to the fats both chemically and biologically, others (like the sterols) showing little direct chemical relation to the fats but apparently bearing significant biological relationships, while still others (like certain of the essential oils) appear to bear little relationship to the fats and to be classified as lipins merely because of their physical properties. If the term "lipins" is to be so broadly used, it may be convenient to apply the term "lipoid" to substances other than fats or fatty acids but which are related to them chemically or biologically.

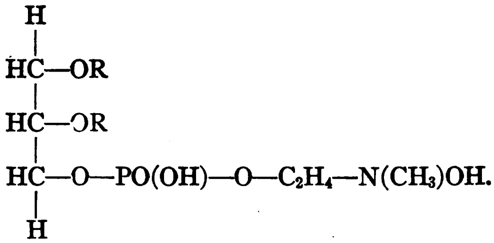
Prominent among the lipoids (or fat-like substances other than true fats) are the *sterols* (solid alcohols) and the *phospholipins* or *phosphatids*. The latter are substances which contain a substituted phosphoric acid radicle in place of one or more of the fatty acid radicles of a fat.

Sterols occur, at least in small amounts, in all natural fats. The best-known sterols are cholesterol ($C_{27}H_{44}O$) and phytosterol ($C_{27}H_{46}O$). Cholesterol occurs in animal fats, and phytosterol (or the closely related sitosterol) in those of vegetable origin. One method of determining whether vegetable fat is present in butter or lard is to examine for the presence of phytosterol, since phytosterol is not, like the substances to which the color reactions of cottonseed and sesame oils are due, carried over from the fat of the food to that of the animal body.

Although its functions are not yet clearly defined, cholesterol appears to be a substance of much physiological significance. The name indicates "bile-solid-alcohol," as it was earliest and best known as a prominent constituent of gall stones. Its deposition in the form of gall stones is attributed to the presence of an insufficient amount of bile salts to keep the cholesterol of the bile in solution. It may also be deposited in the walls of the arteries. As a constituent of the blood cholesterol acts to protect the red blood cells against the action of hemolytic substances, which unless neutralized by cholesterol would tend to cause anemia through excessive destruction of red corpuscles. According to Mathews, cholesterol is one of the most abundant lipins of the brain and occurs in nearly all living tissues; as a constituent of waxes and the sebum of the skin it protects the dermal structures; it, or its degradation products, aids the other lipins in giving to cells their power of holding large quantities of water without dissolving or losing their peculiar semifluid characters; it is believed to be the mother substance from which the bile acids are derived and so plays an important part in the intestinal digestion and absorption of fat; and, on the other hand, cholesterol itself appears to check the action of fat-splitting enzymes in the body and thus to function as a regulator in the metabolism of the cell lipins.

Phospholipins or **phosphatids** are also widely distributed in living cells and doubtless essential to their structure and functions.

Of the phospholipins or phosphatids the best-known are the lecithins, which are abundant in egg yolk and occur also in significant quantities in brain and nerve tissue, blood, lymph, milk, many seeds, and other plant and animal tissues. The structure of lecithin has usually been represented by the formula



$$\begin{array}{l}
\;\;\mathrm{H}\\
\;\;|\\
\mathrm{HC{-}OR}\\
\;\;|\\
\mathrm{HC{-}OR}\\
\;\;|\\
\mathrm{HC{-}O{-}PO(OH){-}O{-}C_2H_4{-}N(CH_3)OH.}\\
\;\;|\\
\;\;\mathrm{H}
\end{array}$$

in which R stands for a fatty acid radicle.

On hydrolysis such a compound would yield glycerol, fatty acids, phosphoric acid, and the nitrogenous base choline (trimethyl oxyethyl ammonium hydroxide). If one of the radicles be that of oleic and the other that of palmitic acid the hydrolysis may be represented thus:

$$C_{42}H_{84}NPO_9 + 4\,H_2O \rightarrow \underset{\text{Glycerol}}{C_3H_8O_3} + \underset{\substack{\text{Oleic}\\ \text{acid}}}{C_{18}H_{34}O_2} + \underset{\substack{\text{Palmitic}\\ \text{acid}}}{C_{16}H_{32}O_2}$$

$$+ \underset{\substack{\text{Phosphor-}\\ \text{ic acid}}}{H_3PO_4} + \underset{\text{Choline}}{C_5H_{15}NO_2}$$

Recent investigations throw doubt upon the view that the nitrogen of typical lecithin is present only as choline groups.

Taylor defines the simpler phosphatids as " lipoids in which two molecules of a higher fatty acid are combined with glycerolphosphoric acid, to which is bound an amino body."

A phosphatid which, like the above, contains one atom of nitrogen and one of phosphorus to the molecule is classified as a monamino-monophospholipin or monamino-monophosphatid. Monamino-diphospholipins, diamino-monophospholipins and triamino-monophospholipins have also been described.

The fat of the active tissues of the body, as distinguished from that of the adipose tissue, seems to consist largely of phospholipins. Thus MacLean and Williams found 84 per cent of the total ether extract of pigs' liver to consist of phospholipins.

Bang holds that it is " no mere coincidence that the most highly organized cells are always richest in lipoids."

Other lipoids may also prove to be of much importance in nutrition. Butter fat and some other natural fats show nutritive functions which cannot be attributed to their glycerides alone and appear to be due to other substances soluble in fats and perhaps of the nature of lipoids. Such as yet unidentified fat-soluble substance appears to be absolutely essential to a fully complete diet since several investigators (Stepp, McCollum and Davis, Osborne and Mendel) have found it impossible to raise young animals to full maturity on rations apparently adequate otherwise but lacking in this "lipoid" of "fat-soluble" factor. These experiments will be cited more fully in connection with the discussion of the specific relations of food to growth (Chapter XIII).

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CHAPTER III

PROTEINS

CARBOHYDRATES and fats are the chief sources of energy for the activities of the body, but not the chief constituents of which the active tissues are composed. Muscle tissue, for instance, is almost devoid of carbohydrate and often contains very little fat. The chief organic constituents of the muscles, and of the protoplasm of plant and animal cells generally, are substances which contain nitrogen and sulphur in addition to carbon, hydrogen, and oxygen. Mulder, in 1838, described a nitrogenous material which he believed to be the fundamental constituent of tissue substances and gave it the name *protein*, derived from a Greek verb meaning " to take the first place." While Mulder's chemical work did not prove to be of permanent value, the term which he introduced has been retained, and in the plural form, *proteins*, is now used as a group name to cover a large number of different but related nitrogenous organic compounds which are so prominent among the constituents of the tissues and of food that they may still be accorded some degree of preeminence in a study of the chemistry of food and nutrition.

Proteins are essential constituents of both plant and animal cells. There is no known life without them. Plants build their own proteins from inorganic materials obtained from the soil and air. Animals form the proteins characteristic of their own tissues, but in general they cannot build them up from simple inorganic substances such as suffice for the plants, and must depend upon the digestion products obtained from the proteins of their food. Since animals must have proteins for the construction and repair or maintenance of their tissues, and since, broadly speaking, they cannot make their proteins except from the cleavage products of other proteins, it follows that proteins are necessary ingredients of the food of all animals.

Chemical Nature and Physical Properties of Proteins in General

Generally speaking, the proteins of different kinds of tissue, and even of the corresponding tissues of different species, are not identical substances. The total number of different proteins occurring in nature must therefore be very great. Of these, some fifty or sixty have been sufficiently isolated and studied to warrant description as chemical individuals. All of these have proven to be very complex substances and in no case has the chemical structure of a natural protein been fully determined. It has, however, been shown that the typical proteins are essentially anhydrides of the following amino acids:

AMINO ACIDS OF COMMON PROTEINS

Monaminomonocarboxylic acids

1 Glycine, amino-acetic acid, $CH_2(NH_2) \cdot COOH$.

2 Alanine, α-amino-propionic acid, $CH_3CH(NH_2) \cdot COOH$.

3 Valine, α-amino-isovaleric acid, $(CH_3)_2CH \cdot CH(NH_2) \cdot COOH$.

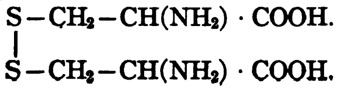
4 Leucine, α-amino-isocaproic acid (α-amino-isobutyl-acetic acid),
$(CH_3)_2CH \cdot CH_2 \cdot CH(NH_2) \cdot COOH$.

5 Phenylalanine, phenyl-α-amino-propionic acid,
$C_6H_5CH_2 \cdot CH(NH_2) \cdot COOH$.

6 Tyrosine, oxyphenyl α-amino propionic acid,
$C_6H_4(OH) \cdot CH_2 \cdot CH(NH_2) \cdot COOH$.

7 Serine, α-amino-β-hydroxy-propionic acid,
$CH_2(OH) \cdot CH(NH_2) \cdot COOH$.

8 Cystine (dicysteine), or di-(α-amino-β-thio-lactic acid),



$$\begin{array}{l} S-CH_2-CH(NH_2) \cdot COOH. \\ | \\ S-CH_2-CH(NH_2) \cdot COOH. \end{array}$$

Monaminodicarboxylic acids

Aspartic acid, amino-succinic acid,

$COOH \cdot CH_2 \cdot CH(NH_2) \cdot COOH.$

Glutamic (glutaminic) acid, amino-glutaric acid,

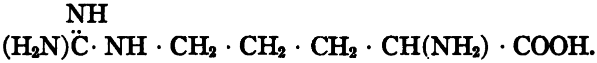
$COOH \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot COOH.$

Diaminomonocarboxylic acids

Ornithine, *α*, *δ*, diamino-valeric acid,

$CH_2(NH_2) \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot COOH.$

Arginine, *δ*-guanidino-*α*-amino-valeric acid,



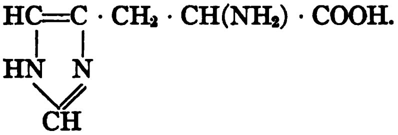
$$(H_2N)\overset{NH}{\ddot{C}} \cdot NH \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot COOH.$$

Lysine, *α*, *ε*, diamino-n-caproic acid,

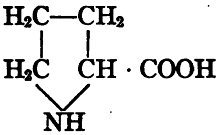
$CH_2(NH_2) \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot COOH.$

Heterocyclic Amino Acids:

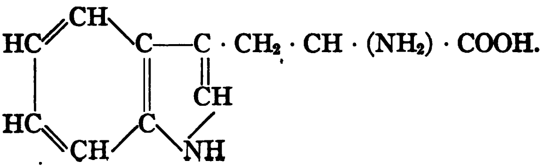
Histidine, *α*-amino-*β*-imidazol propionic acid,



Proline, pyrrolidin-carboxylic acid,

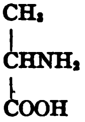


Tryptophane, *α*-amino-*β*-indol-propionic acid,



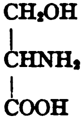
It will be noted that these constituents of the protein molecule differ much in structure among themselves. They are, however, all *α*-amino acids, *i.e.*, the amino group (or one of them if there be more than one) is attached to the carbon atom adjacent to the carboxyl.

In view of the wide occurrence of the alanine radicle in proteins and the frequency with which we shall have occasion to discuss the behavior of alanine (as a typical amino acid) in metabolism, it may be of interest to point out that several of the amino acids, even including some of unique constitution, may be regarded as derived from alanine by the substitution of a simple or complex radicle for one of the hydrogens on the *β* carbon of alanine. Thus by the substitution of an —OH or —SH group one obtains serine or cysteine respectively; by substituting the phenyl or oxyphenyl group, there results phenylalanine or tyrosine; by the imidazole ($C_3H_3N_2$), histidine; by the indol (C_8H_6N) radicle, tryptophane.



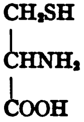
$$\begin{array}{l} CH_3 \\ | \\ CHNH_2 \\ | \\ COOH \end{array}$$

Alanine



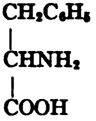
$$\begin{array}{l} CH_2OH \\ | \\ CHNH_2 \\ | \\ COOH \end{array}$$

Serine



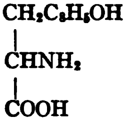
$$\begin{array}{l} CH_2SH \\ | \\ CHNH_2 \\ | \\ COOH \end{array}$$

Cysteine



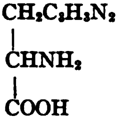
$$\begin{array}{l} CH_2C_6H_5 \\ | \\ CHNH_2 \\ | \\ COOH \end{array}$$

Phenylalanine



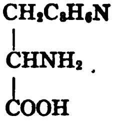
$$\begin{array}{l} CH_2C_6H_4OH \\ | \\ CHNH_2 \\ | \\ COOH \end{array}$$

Tyrosine



$$\begin{array}{l} CH_2C_3H_3N_2 \\ | \\ CHNH_2 \\ | \\ COOH \end{array}$$

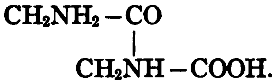
Histidine



$$\begin{array}{l} CH_2C_8H_6N \\ | \\ CHNH_2 \\ | \\ COOH \end{array}$$

Tryptophane

The linkage of the amino acid radicles in the protein molecule is chiefly through the carboxyl group of one amino acid reacting with the amino group of another. Thus two molecules of glycine combined by elimination of one molecule of water yield glycyl-glycine,



$$\begin{array}{l} CH_2NH_2-CO \\ \qquad\qquad\quad | \\ \qquad\quad CH_2NH-COOH. \end{array}$$

which is the simplest of an immense group of anhydrides of amino acids, all of which are called "peptids." Dipeptids contain two amino acid radicles, tripeptids contain three, etc. Fischer, by uniting 7 to 19 amino-acid radicles, has produced synthetic polypeptids which in some of their properties resemble the peptones, the simplest substances usually regarded as true proteins. Peptones are formed in nature by the digestive hydrolysis of ordinary proteins, whose structure is doubtless considerably more complex.

A certain analogy between carbohydrates and proteins may be noted. As starch on hydrolysis yields the polysaccharide dextrins, the disaccharide maltose, and finally as end product the monosaccharide glucose, so the native protein is hydrolyzed through peptones, polypeptids, and di- or tri-peptids, to amino acids. Thus the amino acid bears the same general relation to the protein which glucose bears to starch; and just as the molecular weight of starch is very high and a single starch molecule yields a large (unknown) number of monosaccharide molecules, so the molecular weight of the protein is very high and the protein molecule yields a large (unknown) number of amino acid molecules. There is, however, this important difference: the molecules of monosaccharide resulting from complete hydrolysis of starch are all alike (glucose), whereas the complete hydrolysis of any typical protein yields several of the above-mentioned amino acids, in the case of most proteins from twelve to twenty.

In view of the marked differences in structure existing among these amino acids it becomes important to know the relative proportions in which the various amino acid radicles exist in the different proteins. This is studied by hydrolyzing the protein and separating and recovering as completely as possible the amino acids resulting from the hydrolysis. Since the recovery of the amino acids cannot be accomplished without loss, the results obtained are not strictly quantitative and our knowledge of the radicles which make up the protein molecule remains incomplete. It is believed by the investigators who have given most attention to the question that the failure of the recovered amino acids to show a summation of one hundred per cent is more probably due to unavoidable losses in estimating the known amino acids than to the presence of other amino acids not yet identified. The accompanying table shows the percentages of amino acids obtained from four proteins occurring in different food materials.

Percentages of Amino Acids from Four Different Proteins *

	Casein (from Milk)	Gelatin	Gliadin (from Wheat)	Zein (from Maize)
Glycine	0.00	16.5	0.00	0.00
Alanine	1.50	0.6	2.00	13.39
Valine	7.20	1.	3.34	1.88
Leucine	9.35	9.2	6.62	19.55
Proline	6.70	10.4	13.22	9.04
Aspartic acid	1.39	1.2	0.58	1.71
Glutamic acid	15.55	16.8	43.66	26.17
Phenylalanine	3.20	1.	2.35	6.55
Tyrosine	4.50	0.	1.50	3.55
Serine	.50	.4	.13	1.02
Oxyproline	.23	3.0	—	—
Histidine	2.50	.4	1.84	.82
Arginine	3.81	9.3	3.16	1.55
Lysine	7.61	6.	0.92	0.00
Tryptophane	1.5	0.0	1.0	0.00
Cystine	.06	—	.45	—
Ammonia	1.61	.4	5.22	3.64
Summation	67.21	76.21	85.67	88.87

From the data given in the table it will be seen that the proportions in which a given amino acid radicle occurs in various

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* In general each figure given in the table is the highest of the results reported in recent investigations. This is deemed more accurate than to give average results, because of the unavoidable losses referred to above.

The data given for casein, gliadin, and zein are taken chiefly from the work of Osborne and his associates; those for gelatin chiefly from that of Skraup and Behler.

proteins may be quite different. The four proteins here shown yield from 0.0 to 16.5 per cent of glycine; from 0.6 to 9.8 per cent of alanine; from 1.0 to 7.2 per cent of valine, from 6.6 to 19.6 per cent of leucine. Of lysine, zein yields none, gliadin about 1 per cent, gelatin 6 per cent, and casein about 8 per cent. Of tryptophane, zein and gelatin yield none, gliadin about 1 per cent, casein about 1.5 per cent.

For more detailed comparisons of the percentages of amino acids in different proteins and also in the flesh of four widely separated species, the more extended table further on in this chapter may be consulted. Whether it be essential that the proteins of the food shall furnish all the amino acids which the body proteins contain will naturally depend upon whether the body is able to make individual amino acids or not. Experimental evidence has shown that the animal body can make glycine readily, so that the absence of glycine radicles in the food proteins does not detract from their nutritive value. On the other hand the animal body does not seem able to make tryptophane, and as this is an essential constituent of body tissue the food protein must always furnish tryptophane if it is to meet the needs of animal nutrition. Feeding experiments have also shown that the rate of growth of young animals may be largely influenced by the lysine content of the proteins fed; food proteins in which lysine is lacking or inadequate may suffice for the maintenance of full grown animals but fail to support normal growth in the young of the same species.

Such facts as these make it important that we study the proteins not only as a group but also individually and that we learn as much as possible about the kinds and amounts of amino acid radicles in the individual proteins.

The ultimate composition of the proteins shows a general similarity throughout the group. All contain carbon, hydrogen, oxygen, nitrogen, and sulphur; some also phosphorus or iron.

COMPOSITION OF SOME TYPICAL PROTEINS ACCORDING TO OSBORNE

	CARBON PER CENT	HYDROGEN PER CENT	NITROGEN PER CENT	OXYGEN PER CENT	SULPHUR PER CENT	IRON PER CENT	PHOSPHORUS PER CENT
Egg-albumin .	52.75	7.10	15.51	23.024	1.616		
Lact-albumin .	52.19	7.18	15.77	23.13	1.73		
Leucosin . . .	53.02	6.84	16.80	22.06	1.28		
Serum-globulin	52.71	7.01	15.85	23.32	1.11		
Myosin . . .	52.82	7.11	16.67	22.03	1.27		
Edestin . . .	51.50	7.02	18.69	21.91	0.88		
Legumin . . .	51.72	6.95	18.04	22.905	0.385		
Casein . . .	53.13	7.06	15.78	22.37	0.80	—	0.86
Ovo-vitellin . .	51.56	7.12	16.23	23.242	1.028	—	0.82
Gliadin . . .	52.72	6.86	17.66	21.733	1.027		
Zein	55.23	7.26	16.13	20.78	0.60		
Oxyhemoglobin	54.64	7.09	17.38	20.165	0.39	0.335	—

It will be seen that all these typical proteins contain 51 to 55 per cent carbon, about 7 per cent hydrogen, 20 to 23 per cent oxygen, 15.5 to 18.7 per cent nitrogen, 0.3 to 2.0 per cent sulphur. Other typical proteins thus far studied have shown ultimate composition within these same limits.

Similarity of elementary composition is entirely consistent with the belief that there may be an enormous number of chemical individuals among the proteins of nature.

Fischer has recently illustrated the vast number of isomers which may exist among polypeptids and proteins by pointing out that a synthetic 19-peptid obtained by linking 15 glycine and 4 leucine molecules is only one of 3876 possible isomers, without considering the tautomerism of the peptid linking. When more than two kinds of amino acids are involved, the possible number of isomers increases very rapidly. If a protein be imagined made up of 30 molecules of 18 different amino acids, one taken twice, one 3 times, another 3, one 4, one 5 times, and 13 taken once each, there would be 10^{27} isomers even if there were no tautomerism of the peptid group and if the linking took place only in the simple way as with monamino-monocarboxylic acids.

It is easy to see that when one considers not only isomerism but the vast number of compounds of slightly different composition which can be obtained by varying the kinds and proportions of the amino acid radicals in the protein molecule, the possible number of different proteins of very similar elementary composition is practically unlimited.

Probable molecular weights. — From the results of ultimate analysis an approximate indication of the minimum molecular weight may often be obtained by a very simple calculation. Thus, oxyhemoglobin contains only 0.335 per cent of iron, and since there must be at least one iron atom in the molecule, it is obvious from a simple proportion making use of the atomic weight of iron,

$$0.335 : 56 :: 100 : x,$$

that the molecular weight of hemoglobin must be in the neighborhood of 16,800 or a multiple of this.

To take an example from the simple proteins, zein contains 0.60 per cent of sulphur, of which one third is much more readily split off than the other two thirds, from which it appears that the molecule contains three, or a multiple of three, sulphur atoms. Then by the proportion,

$$0.60 : (32 \times 3) :: 100 : x,$$

it is found that about 16,000 or a multiple thereof is the probable molecular weight of zein.

Estimates of the same order of magnitude are obtained if we base our calculations on the proximate rather than the ultimate analyses of the purified protein preparations. Osborne, Van Slyke, Leavenworth, and Vinograd have recently concluded from a very searching investigation that the lysine content of gliadin must lie between 0.64 and 1.20 per cent. Since the molecular weight of lysine is 146 it follows that the corresponding minimum estimate of the molecular weight of gliadin must fall between 12,000 and 23,000. The experimental facts do not permit the assumption of any lower molecular weight but are not inconsistent with the view that the true molecular weight may be some multiple of this.

Physical properties. — In only a few cases have proteins been obtained in crystalline form. Generally speaking the proteins may be regarded as typically colloidal substances. This does not preclude the belief that in the tissues and fluids of the body the proteins may exist largely in combination with electrolytes. In view of the fact that the behavior of proteins in the tissues is largely dependent upon their colloidal character it is of interest to bear in mind the very high molecular weights of the proteins as mentioned in the last paragraph. Discussions of colloids commonly emphasize the fact that the smallest particles demonstrable under the ultramicroscope must still be of quite a different order of magnitude from that calculated for ordinary molecules. In such a case as that of starch or a typical protein, however, the probable molecular weight is so enormous as to make it a debatable question whether the individual molecules may not constitute colloidal particles when dispersed in water (Bayliss).

The proteins are insoluble in all of the solvents for fats (ether, acetone, chloroform, carbon disulphid, carbon tetrachlorid, benzene, and petroleum distillate). They differ in their solubilities in water, salt solutions, and alcohol, and these differences play a considerable part in the present schemes of classification.

Classification. — There was formerly considerable confusion in the classification and terminology of the proteins and some differences of usage will still be met in the literature. At present, however, the majority of writers follow the recommendations made by a joint committee of the American Physiological Society and the American Society of Biological Chemists in December, 1907. The full text of these recommendations will be found in the appendix. The following is an outline of the classification thus recommended; to which have been added examples covering most of the food proteins thus far described as chemical individuals.

I. Simple Proteins. Protein substances which yield only amino acids or their derivatives on hydrolysis.

(*a*) *Albumins*. Simple proteins soluble in pure water and coagulable by heat. Examples: egg albumin, lactalbumin (milk), serum albumin (blood), leucosin (wheat), legumelin (peas).

(*b*) *Globulins*. Simple proteins insoluble in pure water, but soluble in neutral salt solutions. Examples: muscle globulin, serum globulin (blood), edestin (wheat, hemp seed, and other seeds), phaseolin (beans), legumin (beans and peas), vignin (cow peas), tuberin (potato), amandin (almonds), excelsin (Brazil nuts), arachin and conarachin (peanuts).

(*c*) *Glutelins*. Simple proteins insoluble in all neutral solvents, but readily soluble in very dilute acids and alkalies. The best-known and most important member of this group is the glutenin of wheat.

(*d*) *Alcohol soluble proteins*. Simple proteins soluble in relatively strong alcohol (70–80 per cent) but insoluble in water, absolute alcohol, and other neutral solvents. Examples: gliadin (wheat), zein (corn), hordein (barley), kafirin (kafir corn).

(*e*) *Albuminoids*. These are the simple proteins characteristic of the skeletal structures of animals (for which reason they are also called scleroproteins) and also of the external protective tissues, such as the skin, hair, etc. None of these proteins is used for food in the natural state, but collagen when boiled with water yields gelatin.

(*f*) *Histones*. Soluble in water, and insoluble in very dilute ammonia, and in the absence of ammonium salts insoluble even in an excess of ammonia; yield precipitates with solutions of other proteins and a coagulum on heating which is easily soluble in very dilute acids. On hydrolysis they yield several amino acids, among which the basic ones predominate. The only members of this group which have any considerable importance as food are the thymus histone and the globin derived from the hemoglobin of the blood.

(*g*) *Protamins.* These are simpler substances than the preceding groups, are soluble in water, not coagulable by heat, possess strong basic properties, and on hydrolysis yield a few amino acids among which the basic amino acids greatly predominate. They are of no importance as food.

II. CONJUGATED PROTEINS. Substances which contain the protein molecule united to some other molecule or molecules otherwise than as a salt.

(*a*) *Nucleoproteins.* Compounds of one or more protein molecules with nucleic acid. Examples of the nucleic acids thus found united with proteins are thymo-nucleic acid (thymus gland), tritico-nucleic acid (wheat germ).

(*b*) *Glycoproteins.* Compounds of the protein molecule with a substance or substances containing a carbohydrate group other than a nucleic acid. Example: mucins.

(*c*) *Phosphoproteins.* Compounds in which the phosphorus is in organic union with the protein molecule otherwise than in a nucleic acid or lecithin. Examples: caseinogen (milk), ovovitellin (egg yolk).

(*d*) *Hemoglobins.* Compounds of the protein molecule with hematin or some similar substance. Example: hemoglobin of blood. (The redness of meat is due chiefly to the hemoglobin of the blood which the meat still retains.)

(*e*) *Lecithoproteins.* Compounds of the protein molecule with lecithins or related substances.

III. DERIVED PROTEINS.

1. *Primary protein derivatives.* Derivatives of the protein molecule apparently formed through hydrolytic changes which involve only slight alterations.

(*a*) *Proteans.* Insoluble products which apparently result from the incipient action of water, very dilute acids, or enzymes. Examples: casein (curdled milk), fibrin (coagulated blood).

(*b*) *Metaproteins.* Products of the further action of acids and alkalies whereby the molecule is sufficiently altered to form proteins soluble in very weak acids and alkalies, but insoluble in neutral solvents. This group includes the substances which have been called "acid proteins," "acid albumins," "syntonin," "alkali proteins," "alkali albumins," and "albuminates."

(*c*) *Coagulated proteins.* Insoluble products which result from (1) the action of heat on protein solutions, or (2) the action of alcohol on the protein. Example: cooked egg albumin, or egg albumin precipitated by means of alcohol.

2. *Secondary protein derivatives.* Products of the further hydrolytic cleavage of the protein molecule.

(*a*) *Proteoses.* Soluble in water, not coagulable by heat, precipitated by saturating their solutions with ammonium sulphate or zinc sulphate. The products commercially known as "peptones" consist largely of proteoses.

(*b*) *Peptones.* Soluble in water, not coagulable by heat, and not precipitated by saturating their solutions with ammonium sulphate or zinc sulphate. These represent a further stage of cleavage than the proteoses.

(*c*) *Peptids.* Definitely characterized combinations of two or more amino acids. An anhydride of two amino acid radicles is called a "di-peptid"; one having three amino acid radicles, a "tri-peptid"; etc. Peptids result from the further hydrolytic cleavage of the peptones. As was mentioned above, many peptids have also been made in the laboratory by the linking together of amino acids.

Substances simpler than the peptones but containing several amino acid radicles are often called "polypeptids."

Properties of Some Individual Proteins

Albumins and *globulins* are very often associated, as, for example, in blood serum and in the cell substance. As a rule the albumins are the more abundant in animal fluids, while the globulins predominate over albumins in animal tissues and in plants. There appears to be no sharp dividing line between the albumins and the globulins. While the globulins are insoluble in pure water, a water extract of animal tissue (muscle, for example) will contain, in addition to albumin, a considerable amount of globulin carried into solution by the salts present in the tissue, and if the salts are removed as completely as possible by dialysis, some of the globulin still remains in solution; separations based upon saturation with neutral salts are also apt to be unsatisfactory (Howell).

Notwithstanding these difficulties, a considerable number of individual albumins and globulins have been isolated, purified, and analyzed. In ultimate composition they show a general similarity except that the albumins are richer in sulphur than the globulins.

Several members of each group have also been studied to determine the kinds and amounts of amino acid radicles which they contain, with the results shown in the table on pages 60 and 61. It is of interest to compare the amino acid make-up of typical proteins with their adequacy in nutrition. A few studies of this sort, notably those of Kauffmann with gelatin and Willcock and Hopkins with zein, had been made some years earlier, but much the greater part of our knowledge in this field is due to the recent investigations of Osborne and Mendel (1911 *et seq.*). Rats have been chiefly used as the experimental animal.

Egg albumin, perhaps the most familiar of all proteins and the one most often chosen to illustrate, in the laboratory, the properties of proteins in general, will be seen to yield no glycine but to furnish all the other usual amino acids in quite appreciable proportions. The feeding experiments show that with a diet adequate as regards all other factors animals may be maintained in normal nutrition and young animals may make normal growth with egg albumin as the sole protein food.

Lactalbumin shows this same property in even greater degree. It appears to be the most efficient in supporting growth of all the proteins which have been studied, and this is believed to be due primarily to its high lysine content (see table beyond).

Legumelin and *leucosin* have not yet been studied in feeding experiments of this kind, nor have such experiments been made with *amandin* or *vicilin*.

Only preliminary feeding experiments not entirely successful as regards growth have been reported for *legumin*, *phaseolin*, and *vignin;* but each of the other three vegetable globulins shown — *edestin*, *excelsin*, and *glycinin* — has been found to suffice for maintenance and normal growth when fed as the sole protein in a diet adequate in other respects.* In fact Osborne and Mendel have kept one family of rats through three generations with edestin as a sole protein food.

Glutelins and the *alcohol-soluble proteins* (*prolamins*) are important as constituents of the cereal grains. The best-known examples of the respective groups are glutenin and gliadin of wheat flour. These proteins resemble each other in ultimate composition, but differ not only in solubilities, but also in their cleavage products. They are much the most important of the proteins of the wheat kernel, the gliadin making up about 50 per cent and the glutenin about 40 per cent of the total protein present. The gliadin and glutenin together constitute the gluten of wheat flour.

Glutenin (wheat glutelin) and *maize glutelin* have each been shown capable, in the rat-feeding experiments cited above, of meeting the requirements not only of maintenance but also of normal growth when fed as the sole protein food in diets adequate in other respects.

Gliadin, *hordein*, and the *prolamin of rye*, when fed singly in the same manner, are found capable of maintaining grown rats but not of supporting normal growth. *Zein*, fed alone in similar experiments, did not suffice either for maintenance or for growth. Osborne and Mendel concluded from these experiments that the failure even to maintain the grown animals was due to the absence of tryptophane; while the failure of the rats to grow on gliadin, hordein, or rye prolamin was due to the fact that these proteins either lack lysine or contain it in insufficient quantity. This interpretation was confirmed by later experiments in which they found that adding tryptophane to the zein food made it adequate for maintenance and adding lysine to the gliadin food made it adequate to support growth.

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* Factors necessary to make a diet adequate will be discussed in Chapters XII and XIII, where experiments upon growth will be considered in greater detail.

Gelatin, the only member of the *albuminoids* (*scleroproteins*) which is of practical importance as food, has long been known to be unable to support protein metabolism when fed as the sole protein food. This inadequacy now appears to be due to the absence of tryptophane and tyrosine and perhaps in part also to the fact that some of the other amino acids, cystine and histidine, are furnished by gelatin in only very small proportion. As early as 1905 Kauffmann tried the experiment of living upon a diet in which gelatin was the sole protein, but was supplemented by additions of tyrosine, tryptophane, and cystine. So far as could be determined by a short experiment the addition of these amino acids seemed to make good the deficiencies of the gelatin.

Nucleoproteins are the characteristic proteins of cell nuclei, and are therefore especially abundant in the highly nucleated cells of the glandular organs, such as the thymus, the pancreas, and the liver. They are compounds of simple proteins with nucleic acid or nuclein. The chemical nature of the latter and their behavior in metabolism will be considered in Chapter V.

Phosphoproteins occur especially in milk and eggs, which obviously function in nature to provide the material for growth and development of new animal tissue. The phosphorus, while probably present in the form of a more or less modified phosphoric acid radicle, appears to be more closely bound in these than in the nucleoproteins. Casein of milk and the vitellin of egg yolk (ovo-vitellin) are the most prominent members of the group. These are sometimes classed with simple proteins under the name nucleo-albumins. Phosphoprotein preparations show on analysis small amounts of iron, which has usually been neglected as an impurity but which is not improbably an essential constituent.

Casein and *ovo-vitellin* fed singly as the sole protein of the ration in the experiments by Osborne and Mendel described above have each been found capable of supporting both maintenance and normal growth, as their amino acid make-up and their place in nature would lead us to expect. The curves in Fig. 1 illustrate the rapid growth on casein as compared with the very slow growth on gliadin and the loss of weight when zein was the sole protein food. The rations were alike except

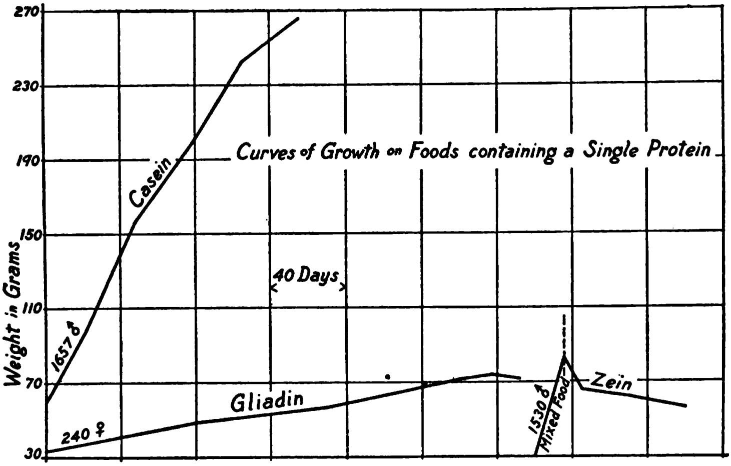

FIG. 1. — Showing typical curves of growth of rats on diets otherwise similar and adequate but containing in each case only a single protein, casein, gliadin, or zein. Courtesy of Dr. L. B. Mendel and the Journal of the American Medical Association.

for the nature of the protein fed; the percentage of protein in the ration was the same in each case.

It will be seen that the rat receiving casein grew over 200 grams in 140 days while the one fed with gliadin grew only 20 grams during the same period. The third rat, which had been growing rapidly on mixed food, began at once to lose weight when put on a ration of which zein was the sole protein.

Hemoglobins, consisting of combinations of simple proteins with coloring matter, serve as carriers of oxygen from the air to the tissues. On boiling or heating with acids or alkalies they are split into their constituent parts: for example, ordinary hemoglobin yields about 4 per cent of hematin, $C_{32}H_{32}N_4FeO_4$, and a residue of globin which was formerly considered a globulin but is now assigned to the histone group.

Proteoses and peptones are products derived from other proteins by digestion or by simple hydrolysis. They are soluble in water and not coagulated by boiling their aqueous solutions. No sharp line can be drawn either between proteoses and peptones, or between peptones and the simpler nitrogen compounds which result from prolonged digestion. As the terms are generally used, peptones may be considered as the products of digestion or hydrolysis which still show the usual color reactions of proteins and are precipitated by strong alcohol; but are not precipitated by saturation of their solutions with zinc or ammonium sulphate, as is the case with proteoses. Proteoses (albumoses) are intermediate products between metaprotein and peptones. In addition to the protein reactions shown by peptones, the proteoses are precipitated from aqueous solutions at ordinary temperatures by adding acetic acid and potassium ferrocyanide, or by saturating the solution with zinc or ammonium sulphate.

The term "peptone" was formerly applied to all digestion products not coagulated by boiling, and is still popularly used in the same sense, the best commercial "peptones" consisting largely of proteoses.

PERCENTAGES OF AMINO ACIDS FROM HYDROLYSIS OF VARIOUS PROTEINS

	ALBUMINS				GLOBULINS							
	Egg Albumin (hen's eggs)	Lactalbumin (cow's milk)	Legumelin (pease)	Leucosin (wheat)	Amandin (almonds)	Edestin (hemp seed)	Excelsin (Brazil nuts)	Glycinin (soy beans)	Legumin (pease)	Phaseolin (white beans)	Vicilin (pease)	Vignin (cow pea)
Glycine	0.00	0.00	0.50	0.94	0.51	3.80	0.60	0.97	0.38	0.55	0.00	0.00
Alanine	2.22	2.50	0.92	4.45	1.40	3.60	2.33	*	2.08	1.80	0.50	0.97
Valine	2.50	0.90	0.69	0.18	0.16	6.20	1.51	0.68	*	1.04	0.15	0.34
Leucine	10.71	19.40	9.63	11.34	4.45	14.50	8.70	8.45	8.00	9.65	9.38	7.82
Phenylalanine	5.07	2.40	4.79	3.83	2.53	3.09	3.55	3.86	3.75	3.25	3.82	5.27
Tyrosine	1.77	4.90	1.56	3.34	1.12	2.13	3.03	1.86	1.55	2.84	2.38	2.26
Serine	*	*	*	*		0.33			0.53	0.38		
Cystine	*	*	*	*		1.00						
Aspartic acid	2.20	1.0	4.11	3.35	5.42	4.50	3.85	3.89	5.30	5.24	5.30	3.97
Glutamic acid	9.10	10.1	12.96	6.73	23.14	18.74	12.94	19.46	16.97	14.54	21.34	16.89
Arginine	4.91	3.23	5.45	5.94	11.85	14.17	16.1	5.12	11.71	4.87	8.91	7.20
Lysine	3.76	9.16	3.03	2.75	0.70	1.65	1.64	2.71	4.98	4.58	5.40	4.28
Histidine	1.71	2.06	2.27	2.83	1.58	2.19	2.50	1.39	1.69	2.62	2.47	3.08
Proline	3.56	4.0	3.96	3.18	2.44	4.10	3.65	3.78	3.22	2.77	4.06	5.25
Oxyproline	*	*	*	*	*	*	*					
Tryptophane	present	3.	present	present	present	present	present	present	present	present	present	present
Ammonia	1.34	1.32	1.26	1.41	3.70	2.28	1.80	2.56	2.05	2.06	2.03	2.32
Summation	48.85	63.97	51.13	50.27	59.00	82.28	62.20	54.73	62.21	56.19	65.74	59.65

* Not determined.

PERCENTAGES OF AMINO ACIDS FROM HYDROLYSIS OF VARIOUS PROTEINS

	GLUTELINS		ALCOHOL-SOLUBLE PROTEINS				ALBUMINOID	PHOSPHOPROTEINS		FLESH (NOT SINGLE PROTEINS)			
	Glutenin (wheat)	Maize Glutelin	Gliadin (wheat)	Hordein (barley)	Prolamin of Rye	Zein (maize)	Gelatin	Casein (cow's milk)	Ovovitellin (hen's eggs)	Beef	Chicken	Halibut	Scallop
Glycine . .	0.89	0.25	0.00	0.00	0.13	0.00	16.5	0.00	0.00	2.06	0.68	0.00	0.00
Alanine . .	4.65	?	2.00	0.43	1.33	13.39	1.6	1.50	0.75	3.72	2.28	—	—
Valine . . .	0.24	?	3.34	0.13	—	1.88	1.0	7.20	1.87	0.81	—	0.79	—
Leucine . .	5.95	6.22	6.62	5.67	6.30	19.55	9.2?	9.35	9.87	11.65	11.19	10.33	8.78
Phenylalanine	1.97	1.74	2.35	5.03	2.70	6.55	1.0	3.20	2.54	3.15	3.53	3.04	4.90
Tyrosine . .	4.25	3.78	1.50	1.67	1.19	3.55	0.0	4.50	3.37	2.20	2.16	2.39	1.95
Serine . .	0.74	?	0.13	?	0.06	1.02	0.4	0.50	?	?	?	?	?
Cystine . .	0.02	*	0.45	1.00	*	*	—	0.06	*	?			
Aspartic acid	0.91	0.63	0.58	?	0.25	1.71	1.2	1.39	2.13	4.51	3.21	2.73	3.47
Glutamic acid	23.42	12.72	43.66	43.20	38.05	26.17	16.8	15.55	12.95	15.49	16.48	10.13	14.88
Arginine . .	4.72	7.06	3.16	2.16	2.22	1.55	9.3	3.81	7.46	7.47	6.50	6.34	7.38
Lysine . .	1.92	2.93	0.92	0.00?		0.00	6.0	7.61	4.81	7.59	7.24	7.45	5.77
Histidine . .	1.76	3.00	1.84	1.28	0.39	0.82	0.4	2.50	1.90	1.76	2.47	2.55	2.02
Proline : .	4.23	4.99	13.22	13.73	9.82	9.04	10.4	6.70	4.18	5.82	4.74	3.17	2.28
Oxyproline .							3.0	0.23					
Tryptophane	present	present	1.0	present	present	absent	absent	1.50	present	present	present	present	present
Ammonia .	4.01	2.21	5.22	4.84	5.11	3.64	0.4	1.61	1.25	1.07	1.67	1.33	1.08
Summation .	59.68	45.53	85.99	79.14	67.55	88.87	77.2	67.21[1]	53.08	67.30	62.15	50.25	52.51

* Not determined in these cases and presumably not, in the cases left blank. In other cases the figures given for cystine may be much too low because of decomposition of this amino acid in the process of hydrolyzing the protein.

[1] Fischer and Abderhalden report also diamino-trioxy-dodecanic acid 0.75 %.

Relation between Chemical Constitution of the Proteins and Their Food Value

Several facts bearing upon the relation between the feeding values of individual proteins and their amino acid make-up have been cited in the preceding pages. The subject is of great importance and is now under active investigation. Since the experimental facts are still being determined, any attempt to generalize broadly at this point would be premature. A few important conclusions may, however, be deduced from the facts already given.

Glycine, although an essential constituent of body tissue, need not be furnished by the food, for several proteins which do not yield glycine on hydrolysis have been shown to be adequate when fed as sole protein of an experimental ration. It appears therefore that supplies of glycine fully adequate to meet all normal needs may be formed within the body itself.

Tryptophane, on the other hand, apparently must always be supplied to the animal body; food furnishing no tryptophane has always proven inadequate even for maintenance of full-grown animals. Apparently the animal body is unable to make tryptophane (or at least to make it at the rate required for normal metabolism) and proteins lacking the tryptophane radicle must be regarded as always inadequate as a sole protein food.

Lysine, again, is especially important in connection with growth. Proteins which yield little, if any, lysine (and which are otherwise adequate in their amino acid make-up) appear to suffice as the sole protein food in the maintenance of full-grown animals (rats) but not to support a normal growth of the young.

As regards the influence of the presence or absence of glycine, lysine, and tryptophane radicles in the protein molecule, it seems possible to correlate the chemical structure and the nutritive value of the proteins quite definitely. In establishing this correlation, Osborne and Mendel have made one of the most important advances in the entire development of the chemistry of food and nutrition.

That the inadequacy of zein for maintenance is essentially due to the lack of tryptophane, they demonstrated by feeding a ration with zein as sole protein but with tryptophane added. This mixture permitted maintenance without growth (rat 1892, middle portion of Fig. 2). Then by the addition of lysine to the zein and tryptophane diet they induced normal growth as shown by the continuation of the weight curve of rat 1892 at the right of Fig. 2. In another case (rat 1773, at the left of Fig. 2) a rat which was rapidly losing weight on the zein diet was restored to a condition of normal growth by the addition of tryptophane and lysine to the food.

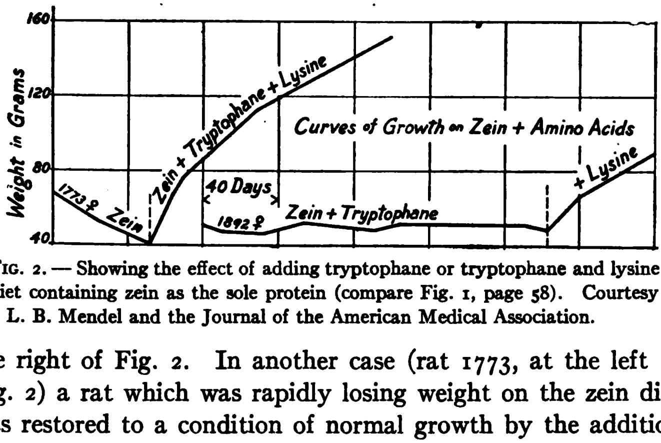

FIG. 2. — Showing the effect of adding tryptophane or tryptophane and lysine to a diet containing zein as the sole protein (compare Fig. 1, page 58). Courtesy of Dr. L. B. Mendel and the Journal of the American Medical Association.

As Mendel expresses it: "If we analyze the situation as revealed in the charts of some actual experiments, it becomes apparent that both lysine and tryptophane are unquestionably necessary as constructive units in growth. The decline brought about by the zein food can be stopped by the addition of tryptophane, as such, to the diet. This results in maintenance; but no growth ensues until lysine also is added."

Osborne and Mendel also showed that the addition of lysine to the gliadin ration made it adequate to support normal growth. They have also shown that retardation of growth may sometimes be due to restricted intake of some amino acid other than lysine.

In the experiments above described the rations always contained a liberal amount (usually 18 per cent) of protein. If, on the other hand, the percentage of protein in the food be sufficiently reduced, the growth may be retarded even though the protein be of a kind which is entirely adequate when liberally fed. Thus on a ration containing 9 per cent of casein the rats grew only about half as rapidly as when they received 18 per cent;* and in this case the limiting factor was not lysine but

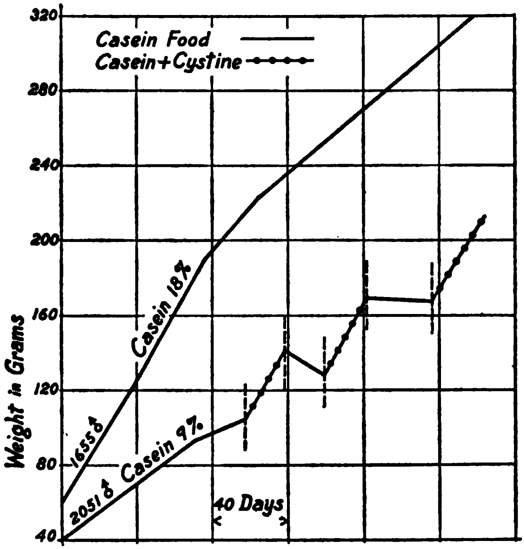

FIG. 3. — Showing that the insufficiency of a low-casein diet was essentially due to its relative deficiency in cystine. Courtesy of Dr. L. B. Mendel and the Journal of the American Medical Association.

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* On account of the very different rates of growth, not to mention other differences between the species, one must not attempt to apply the quantitive data of the rat-feeding experiments directly to the problem of protein requirement in man.

cystine, for the addition of cystine to the low-casein diet induced a normal rate of growth which was immediately checked when the cystine was withdrawn and resumed when the cystine was again added to the ration (Fig. 3).

In all of the experiments cited thus far each ration contained only a single isolated protein. This is the ideal condition for the experimental comparison of individual proteins, but is quite different from ordinary or "practical" conditions, since our common protein foods all contain mixtures of proteins, so that even if only a single article of food were consumed the diet would still furnish more than one protein at a time. By feeding definite mixtures of pure proteins Osborne and Mendel have beautifully demonstrated the way in which proteins supplement each other in nutrition. Thus zein alone is, as we have seen, always inadequate as a sole protein food; lactalbumin is adequate when fed in sufficient quantity but when constituting only 4.5 per cent of the food mixture of rats it supports only slow growth; but a food mixture containing 4.5 per cent of lactalbumin and 13.5 per cent of zein supports growth at a fully normal rate (Fig. 4). This shows that a relatively small amount of lactalbumin (one fourth of the protein fed) sufficed to furnish the amino acid groups which the zein lacked. It shows also that zein, which when fed as a sole protein is insufficient even for maintenance, is able as a constituent of a proper food mixture to take part in supplying the materials for growth, to such an extent as to more than double the growth-rate. Thus zein, although inadequate for either maintenance or growth when isolated and fed alone, may nevertheless take an important part in both maintenance and growth when fed as a part of a proper mixed diet. Moreover it may not even be necessary to resort to a mixture of food materials in order to make good the deficiencies of the individual incomplete protein. Corn (maize) itself, along with zein, contains an almost equal amount of another protein, maize glutelin, which Osborne and Mendel have shown to be capable of supporting a normal rate of growth —not to mention the proteins in the embryo of the maize kernel which appear to have a still higher nutritive efficiency (Hart and Humphrey; McCollum and Davis).

Thus it is plain that the mixtures of proteins contained in different articles of food as we eat them do not differ in such a striking way as do the individual proteins when isolated and fed singly; but neither is it true that the proteins of different articles of food are equivalent for all practical purposes. Hart, McCollum, and their associates have shown that the natural protein mixture of milk is more efficient than an equal weight of the mixed proteins of wheat or corn (maize) both for the support of growth in young animals (pigs) and as food for the pro-

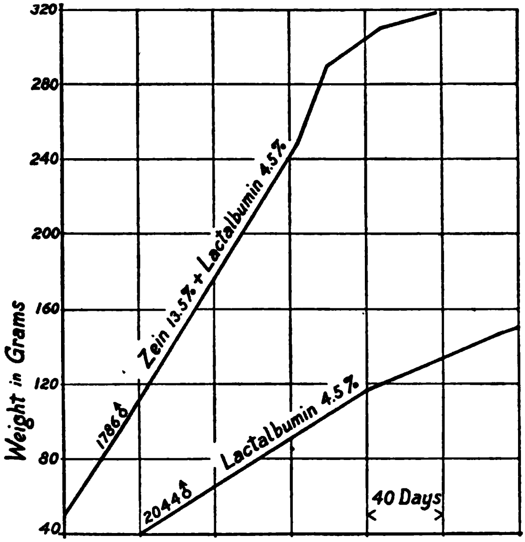

FIG. 4. — Showing the efficiency of lactalbumin as a supplement to zein, and also that zein may take an important part in growth although zein *alone* is inadequate either for growth or maintenance. Courtesy of Dr. L. B. Mendel and the Journal of the American Medical Association.

duction of milk in dairy cattle. While it is always possible that in comparisons between natural food materials the results may be influenced by differences in the unknown food constituents which may be present, yet in the cases here cited it is probable that the differing efficiencies ascribed to milk and grain proteins are mainly due to the same differences of chemical constitution ("amino acid make-up") to which are attributable the striking results obtained in the experiments previously cited in which isolated foodstuffs were fed.

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CHAPTER IV

ENZYMES AND DIGESTION

THE carbohydrates, fats, and proteins as they exist in foods* are in most cases not of a nature to be used by the body tissues in the exact form in which they are eaten, but must usually undergo more or less alteration in the digestive tract to fit them for absorption and utilization. In so far as the changes which the food undergoes in the alimentary tract are chemical they are brought about mainly by the action of digestive enzymes; but the efficiency of the digestive process is also largely dependent upon the mechanical factors of digestion which therefore will also be briefly considered in this chapter.

Historical

The idea that changes comparable to fermentation are involved in the processes of digestion apparently originated with von Helmont about 300 years ago. Sylvius, half a century later, cited alcoholic and acetous fermentations to illustrate the type of process by which he believed the foodstuffs to be digested. Descartes held that as the result of a peculiar fermentation there was generated in the stomach "an acid of great potency, comparable to nitric acid." From the standpoint of our present knowledge these early scientists appear to have made considerable progress toward a correct interpretation of the digestive process; but in their own times, before the beginning of the scientific development of organic or physiological chemistry, the views which they advanced appeared hazy and unscientific compared with those of the physiologists who were studying digestion from the mechanical point of view and by supposedly exact methods. Thus Dr. Archibald Pitcairn (1652–1713) proposed to explain gastric digestion, " without the aid of a Dæmon or a Stygian Liquor," as due entirely to the triturating action of the stomach, the power of whose muscular walls he estimated as " equal to 12,951 pounds " (Gamgee).

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* A table showing percentages of proteins, fats, and carbohydrates in foods is given in Appendix B.

The view that the digestion of food in the stomach is due solely to the mechanical action of the stomach walls was refuted by Réaumur, working with birds, and by Stevens, who experimented with a man who was accustomed to swallow small stones and regurgitate them at will. In Stevens' experiments this man swallowed hollow silver balls filled with food and perforated to permit access of the gastric juice but strong enough to resist the muscular contractions of the stomach walls. Food thus introduced was found to undergo digestion in the stomach although it was entirely protected from the triturating action of the stomach walls. Furthermore Stevens found that gastric juice obtained from a dog was able to digest meat outside of the stomach. At about the same time Spallanzani also showed clearly that gastric juice can act outside of the body. In addition, he pointed out its antiseptic properties and emphasized the difference between the digestive process and that of alcoholic, acid, or putrefactive fermentation. About fifty years after the work of Spallanzani came the classical observations (1825–1833) of Dr. Beaumont upon Alexis St. Martin, who, as the result of a gunshot wound, was left after recovery from his injury with a gastric fistula which permitted both the collection of human gastric juice and the direct observation of the processes going on in the stomach of a healthy man "active, athletic, and vigorous, exercising, eating, and drinking, like other healthy and active people." Dr. Beaumont's full and interesting account of his experiments with St. Martin[1] greatly extended the knowledge both of the muscular behavior of the stomach and of the conditions governing the secretion of the gastric juice and the " chymification " of the food in the stomach. The year after the publication of Beaumont's observations, Eberle showed[2] that by extracting the mucous membrane of the stomach with dilute hydrochloric acid he could obtain an artificial juice which showed the same digestive action which Spallanzani and Beaumont had observed with the natural secretion, and two years later Schwann[3] concluded that gastric juice owed its peculiar activity to a substance presumably different from any substance previously known and to which he gave the name *pepsin*. Schwann did not claim to have isolated this peculiar substance in a pure state but did effect a partial separation. Subsequently several other investigators attempted to isolate pepsin.

Attempts to Determine the Chemical Nature of Enzymes[*]

In 1902 Pekelharing prepared what has generally been regarded as probably the purest pepsin of which we have record. This product contained carbon, hydrogen, nitrogen, and sulphur in proportions within the range of variation found among ordinary proteins.[†] It also behaved like ordinary proteins in the xanthoproteic test and Millon reaction and in showing the presence of the tryptophane group.

[1] W. Beaumont. *Experiments and Observations on the Gastric Juice and the Physiology of Digestion*. Plattsburg, 1833.

[2] Eberle. *Physiologie der Verdauung nach Versuchen*. Würzburg, 1834.

[3] Schwann. *Ueber das Wesen der Verdauungsprocesse*. Müller's *Archiv*, 1836, pages 90–138.

[*] Those students not yet familiar with the names of the common enzymes should perhaps read first the sections on classification and terminology below.

[†] A small amount of chlorine shown by Pekelharing's preparation was later found by Dezani to be not an essential constituent but probably due to incomplete removal of the hydrochloric acid with which pepsin is associated in the gastric juice.

Dezani, in 1910, carried forward the work upon the chemical nature of pepsin by preparing what was believed to be a substantial duplicate of Pekelharing's product and submitting this to hydrolysis, followed by search for individual hydrolytic products according to the methods which had recently been developed in the study of the structure of the proteins. He demonstrated the presence of leucine, tyrosine, arginine, histidine, and lysine and also found evidence of other amino acids which the limitations of his material and methods did not permit him to identify.

Thus pepsin as prepared by Pekelharing and by Dezani is a nitrogenous material not identical with any other known substance but complying with the criteria of our present conception of a protein in elementary composition, in color reactions, and especially in yielding the familiar amino acids upon hydrolysis. Recent studies by Aldrich also indicate that the chemical nature of pepsin is that of a protein.

It must be borne in mind that the criteria of purity usually applied in chemical investigations are not applicable to enzyme preparations because of their colloidal nature and the readiness with which their characteristic properties are destroyed. Yet in view of the fact that, with very few if any exceptions, the changes by which the organic foodstuffs are prepared for absorption in the digestive tract and are utilized in the body tissues are dependent upon the presence of enzymes the material for whose synthesis must in the long run be furnished by food, we should not be deterred by the inherent difficulties and uncertainties of the subject from the study of such evidence regarding the chemical nature of the enzymes as can be obtained; nor are we at present quite so much in the dark as the statements in most textbooks would seem to indicate.

Several years earlier than Pekelharing's work on pepsin, Osborne[1] had published an investigation of the chemical nature of diastase (malt amylase), which may be regarded as marking the beginning of our modern knowledge in this field. From this work it appeared that the enzymic activity is a property of a definite fraction of the protein material of the malt, or in other words that the enzyme is protein in its chemical nature. Although criticized by some, Osborne's findings have been confirmed by the most recent investigations. Since space permits here only the discussion of those enzymes which are directly concerned in digestion, the reader must be referred to the original papers for an account of Osborne's methods and results.

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[1] T. B. Osborne. *Journal of the American Chemical Society*, Vol. 17, page 587 (1895); Vol. 18, page 536 (1896).

Of the two amylases concerned in the digestive process, ptyalin of saliva and amylopsin of the pancreatic juice, only the pancreatic amylase has been studied by modern methods with reference to its chemical nature.

In an investigation[1] in which the attempts at purification were guided and their success largely judged by quantitative determinations of the starch-digesting action of the products there was developed a method of purification which in numerous independent experiments yielded a product that was not only extraordinarily active in the hydrolysis of starch but was essentially uniform both in digestive activity and in chemical nature. This result strongly suggests that the product was not merely an indefinite mixture but represented at least some approximation toward an actual isolation of the enzyme. These preparations show the composition and color reactions of typical proteins and, like Osborne's malt amylase, the material when heated in water solution yields an albumin coagulum and a proteose or peptone which remains in solution. Moreover, on hydrolysis the material yields the same groups of amino acids which are yielded by typical proteins such as casein, which it also resembles in elementary composition.

While the chemical nature of the lipases of the digestive tract has not been studied, Falk and Sugiura have shown that the purified lipase preparations made from castor beans are, like the proteases and amylases above mentioned, essentially protein material.*

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[1] *Journal of the American Chemical Society*, Vol. 33, page 1195; Vol. 34, page 1104; Vol. 35, page 1790.

The materials obtained in attempts to isolate enzymes are here called merely products or preparations; it is not stated that any enzyme has been perfectly separated and purified. As already explained, the familiar criteria of purity are not applicable to these unstable colloidal substances. It is possible that the enzymes in the purified preparations mentioned above may still be mixed with considerable amounts of other substances, and it has even been suggested that the protein material of which the above-mentioned enzyme preparations are chiefly composed may be present only as a carrier and that the actual enzyme may be a substance of a different nature. There is, however, no direct evidence in favor of this suggestion. The facts now available make it altogether probable that the typical enzymes concerned in the utilization of the foodstuffs either are modified proteins or contain protein as an essential component. In this case the food protein must furnish material for body enzymes as well as for body tissue.

Classification and General Properties of Enzymes

The word "enzyme" (from the Greek "in yeast") was introduced by Kühne as a general designation for the substances formed in plants or animals which had previously been called

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* Recently Falk has suggested that the lipolytically active grouping is the tautomeric enol-lactim form of the peptide linking which becomes inactive on rearrangement to the keto form. Experiments testing this view resulted in the production of lipolytically active substances by the action of alkali on castor bean globulin, casein, and gelatin. Further confirming evidence was obtained on studying the ester-hydrolyzing action of glycine, glycyl-glycine, and hippuric acid at different hydrogen ion concentrations. Falk holds that "given a definite chemical grouping, the nature of which has been indicated, and which may be present in different classes of substances, certain definite lipolytic actions will result."

"soluble" or "unorganized" ferments to distinguish them from "organized" ferments (fermentation organisms). As more and more of the activities previously regarded as characteristic of organisms have been found to be due to enzymes, the conception of enzyme action has broadened until now the term enzyme is applied by most writers to all organic catalysts formed in plant or animal cells. Those which are ordinarily secreted from the cell and exert their activities outside of it (as in the case of the digestive ferments) are sometimes called *extracellular* enzymes, and those which normally perform their functions within the cells in which they are formed (as in yeast or in muscle cells) may be called *intracellular* enzymes even though it be possible by artificial means to cause them to act independently of living matter. Although each enzyme is generally supposed to be a definite chemical substance, the identification and classification of enzymes are based upon the changes which they bring about. Some of the better-known groups of enzymes are as follows:

1. The hydrolytic enzymes.
    a. Proteolytic or protein-splitting enzymes.
    b. Lipolytic or fat-splitting enzymes.
    c. Amylolytic or starch-splitting enzymes.
    d. Sugar-splitting enzymes.
2. The coagulating enzymes, such as thrombin or thrombase (the fibrin ferment), and rennin, which causes the clotting of milk.
3. The oxidizing enzymes, or "oxidases" (which, if the oxidation be accompanied by a splitting off of amino groups, may be called "deamidizing" or "deaminizing" enzymes).
4. The reducing enzymes or "reductases."
5. Those which, like the zymase of yeast, produce carbon dioxide without using free oxygen.
6. Enzymes causing a breaking down of a larger into a smaller molecule of the same composition, as in the production of lactic acid from glucose.

7. Enzymes causing chemical rearrangement without breaking down of larger into smaller molecules, "mutases."

Terminology of the hydrolytic enzymes. — Except in so far as some familiar enzymes continue to be known by their old established names (pepsin, rennin, trypsin, etc.), scientific usage now generally follows the suggestion of Duclaux that each hydrolytic enzyme be designated by a name indicating the kind of substance on which it acts, together with the suffix *ase*. Thus starch-splitting enzymes are called *amylases;* fat-splitting enzymes, *lipases;* protein-splitting enzymes, *proteases*. The name showing the activity of the enzyme is often preceded by an adjective to indicate its source; *e.g. salivary amylase* (ptyalin), *pancreatic amylase* (amylopsin). Such designation does not necessarily imply that the amylase found in the saliva either is or is not the same substance as the amylase of the pancreatic juice.

In discussions of enzyme action the substance on which the enzyme acts is sometimes called the *substrate*.

Within the cell producing it an enzyme often exists in an inactive form known as the *zymogen* or antecedent of the active enzyme. The zymogen may be stored in the cell in the form of material which is converted into active enzyme at the time of secretion, or the secretion may be poured out with the zymogen not yet completely changed to active enzyme, or sometimes in a form which requires the presence of some other substance in order to render it active. In this case the latter substance is said to *activate* the enzyme.

Influence of hydrogen ion concentration. — The activity of most enzymes is largely dependent upon the exact acidity or alkalinity of the medium. This is now usually expressed in terms of hydrogen ion concentration. Thus a normal solution of hydrochloric acid would contain, if the HCl were completely ionized, 1 gram of hydrogen ions per liter; and in a thousandth-normal solution in which the ionization actually is almost complete (actually about 99 per cent of the HCl in such a solution is ionized at ordinary temperatures) the concentration of hydrogen ions is 0.001 gram per liter or 1×10^{-3}. Pure water, according to the usually accepted estimates, has a hydrogen ion concentration of 1×10^{-7} and the same concentration of hydroxyl ions. Thus water which is pure and strictly neutral may also be regarded as being equivalent to a ten-millionth-normal acid and at the same time a ten-millionth-normal alkali. In order to avoid cumbersome numbers Sorensen has proposed to indicate hydrogen ion concentration by writing the ***negative exponent*** as a whole number, *e.g.* in the case of pure water $P_H^+ = 7.0$; in thousandth-normal hydrochloric acid $P_H^+ = 3.0$. Thus according to the Sorensen notation, generally indicated by the use of the symbol P_H^+, a number lower than 7 shows acidity and the more acid the solution the lower the number; a number higher than 7 shows alkalinity and the greater the alkalinity the higher the P_H^+ number, since this is the negative exponent of the hydrogen ion concentration.

It must be remembered that the Sorensen exponent, or P_H^+ number, varies with the hydrogen ion concentration not arithmetically but logarithmically: $1 \times 10^{-6} = P_H^+\ 6.0$; $2 \times 10^{-6} = P_H^+\ 5.7$.

The hydrogen ion concentrations most favorable to the action of certain well-known enzymes have recently been measured with the following results:

Enzyme	Optimum H Ion Concentration as P_H^+	
Invertase (Sucrase).	4.4	(Nelson)
Pepsin	1.5	(Okada)
Trypsin	8.0–8.3	when acting on fibrin (Long)
Trypsin	5.6–6.3	when acting on casein (Long)
Malt amylase . .	4.4	(Sherman and Thomas)

Activity of the Digestive Enzymes

That the typical digestive enzymes are very pronounced catalysts may be judged from the relatively large amounts of material which they are capable of digesting under favorable conditions. Thus Hammarsten's rennin coagulated 400,000 to 800,000 times its weight of casein; Petit described a pepsin powder which dissolved 500,000 times its weight of fibrin forming 1000 times its weight of peptone; the pancreatic amylase preparation of Sherman and Schlesinger digested 2,000,000 times its weight of starch with the production of 1,200,000 times its weight of maltose.

A catalyzer is usually considered to alter the velocity of a reaction but not to initiate it. Thus hydrogen peroxide decomposes spontaneously into water and oxygen. In a pure aqueous solution this change goes on slowly, but it is very greatly accelerated by the presence of a minute amount of colloidal platinum. Blood and tissue extracts contain enzymes which accelerate the decomposition of hydrogen peroxide apparently in much the same way as does platinum, and the present tendency is to regard the enzymes generally as acting quite like the inorganic catalyzers in altering by their presence the velocity of certain reactions. Some of the best-known enzyme actions, however, fit into this view only theoretically; for if the enzyme be considered as simply accelerating a reaction already taking place, it must also be considered that in the absence of the enzyme the reaction is so slow that it cannot be demonstrated.

It may perhaps be asked why, if enzymes act by catalysis, there should be any limit to the amount of substrate which the enzyme can hydrolyze. One reason that enzymes cannot hydrolyze infinite amounts of substrate is that they are themselves unstable organic substances which undergo decomposition when kept in solution. In most cases the purer the enzyme the more rapidly its solutions lose their activity. Another reason that an enzyme does not continue to hydrolyze substrate indefinitely is that the reaction is progressively retarded by the accumulation of the products formed.

The activity of an enzyme may be stopped, even when all other conditions are favorable, by the accumulation of the product of its action; and in certain circumstances the action of the enzyme may be reversed so as to accelerate a change in the opposite direction to that in which it ordinarily acts. Thus Croft Hill showed it to be possible to reverse the ordinary action of maltase so as to make it bring about a conversion of mono- into di-saccharide; Pottevin synthesized triolein by means of the pancreas ferment, and Taylor and others have demonstrated a partial reversion of the tryptic digestion of proteins. While the exact significance of these experiments upon the reversibility of the actions brought about by the digestive enzymes has been questioned, there seems to be no doubt that hydrolytic enzymes are widely distributed in active cells and that many of the transformations which take place in the course of the metabolism of the foodstuffs in the body are best explained on the ground of the reversibility of enzyme action. Consideration of the tissue enzymes will be left until the study of the fate of the foodstuffs in metabolism is taken up. At this point it may be convenient to summarize in tabular form the occurrence and action of the chief digestive enzymes.

SUMMARY OF CHIEF DIGESTIVE ENZYMES

ENZYMES		WHERE CHIEFLY FOUND	ACTION
Act on Carbohydrates	Ptyalin (salivary amylase)	Salivary secretions	Converts starch to maltose
	Amylopsin (pancreatic amylase)	Pancreatic juice	Converts starch to maltose
	Invertase (Sucrase)	Intestinal juice	Converts sucrose to glucose and fructose
	Maltase	Intestinal juice	Converts maltose to glucose
	Lactase	Intestinal juice	Converts lactose to glucose and galactose
Act on Fat	Lipases	Gastric (?) and pancreatic juices	Split fats to fatty acids and glycerol

Summary of Chief Digestive Enzymes (*Continued*)

Enzymes		Where Chiefly Found	Action
Act on Proteins	Pepsin	Gastric juice	Splits proteins to proteoses and peptones
	Trypsin	Pancreatic juice	Splits proteins to proteoses, peptones, polypeptids, and amino acids
	Erepsin	Intestinal juice	Splits peptones to amino acids and ammonia

With this brief sketch of the nature and action of the digestive enzymes, the adequate discussion of which would require a volume in itself, we may now pass to a review of the digestive process, following the course of the food through the human alimentary tract and noting briefly both the mechanical and chemical treatment to which it is subjected.

Salivary and Gastric Digestion

Since the muscular movements of the digestive tract, particularly of the stomach when empty, play an important part in bringing about the sensations which lead to the taking of food, it may be well to note at this point the results obtained by Cannon and Washburn in their recent investigation of hunger. Lest hunger be confused with appetite, it is essential to clearness that these terms be defined. Some consider that the two experiences differ only quantitatively, appetite being regarded as a mild state of hunger; but Cannon and Washburn hold that hunger and appetite are fundamentally different. In their view:

"Appetite is related to previous sensations of the taste and smell of food; it has therefore, as Pawlow has shown, important psychic elements. It may exist separate from hunger, as, for example, when we eat delectable dainties merely to please the palate. Sensory associations, delightful or disgusting, determine the appetite for any edible substance, and either memory or present stimulation can thus arouse desire or dislike for food."

" Hunger, on the other hand, is a dull ache or gnawing sensation referred to the lower midchest region or epigastrium. It is the organism's first strong demand for nutriment, and, not satisfied, is likely to grow into a highly uncomfortable pang, less definitely localized as it becomes more intense. It may exist separate from appetite, as, for example, when hunger forces the taking of food not only distasteful but even nauseating."

Hunger is not due merely to emptiness of the stomach. It is true that under ordinary conditions hunger is apt to appear soon after the last food has passed from the stomach to the intestine, but if the stomach be artificially emptied, the sensation of hunger may not be felt until some hours afterward. Nor is hunger due to hydrochloric acid secreted into an empty stomach, for if the empty stomach of a hungry person be washed out, but little if any acid is found.

The explanation of hunger, advanced by Cannon and Washburn, is that it is due to the muscular contractions of the walls of the empty stomach.

In order to learn whether direct proof of this might be secured experimentally in man, one of the investigators accustomed himself to swallowing a small soft rubber balloon attached to the end of a rubber tube by means of which it could be withdrawn when desired. The tube and bulb were habitually carried thus in the esophagus and stomach for two or three hours at a time until the experience ceased to have any disturbing effect. Experiments were then made in which the balloon, thus held in the stomach, was partially inflated with air and connected with a manometer and recording apparatus by means of which any pressure exerted upon the balloon was recorded automatically. In the actual experiments, the subject sat at rest with his hand on a key which he pressed whenever he experienced the sensation of hunger. This key was connected with a recording device which, like the apparatus recording the muscular contractions of the stomach upon the rubber balloon, was out of sight of the subject.

Before hunger was experienced the recording apparatus revealed no evidence of muscular activity in the stomach. The records of hunger "pangs" and of muscular contractions of the stomach were always approximately simultaneous, that is, when the subject of the experiment felt hungry, powerful contractions of the stomach were always being registered. The contractions were about 30 seconds in duration, with pauses of 30 to 90 seconds between. It was found in almost every case that the contraction reached its greatest intensity just before the record of the hunger sensation began, and that the feeling of hunger disappeared when the contraction ceased although no food or drink had been taken. Cannon considers the evidence conclusive that hunger is caused by the contractions, and not vice versa, as Boldireff had thought. Other observations in the course of Cannon's experiments showed that the lower end of the esophagus also contracts periodically in hunger, an explanation of the fact that sensations of hunger may be felt in cases where the stomach has been removed. Furthermore Cannon considers that vague sensations of hunger may also originate from muscular contractions in the intestine.

What causes the stomach contractions which give the sensation of hunger has not been determined. They do not seem to be directly related to bodily need. That they usually begin at or soon after the accustomed meal hour may be taken not only as evidence that habit plays an important rôle, but also as an indication of the desirability of eating at regular times; for in view of the importance of the muscular tone of the stomach walls, these observations seem to justify the view that the strong muscular contraction of the empty stomach may be regarded as an indication that the condition which causes the first sensation of hunger is that in which the stomach is in the best state of readiness to receive the food. There is also direct experimental evidence that the stomach digests more expeditiously the food which is "eaten with hunger" (Hudek and Stigler, cited by Carlson). The description of the digestive process which follows presupposes that the food is eaten under favorable conditions and received by a digestive tract which has been permitted to form good and regular habits.

The eating of food induces a flow of saliva from great numbers of minute glands in the lining membrane of the mouth and from the three pairs of large salivary glands. That saliva is secreted in response to psychic as well as chemical stimulation is shown by the fact that actual contact with the food is not necessary, since secretion may be started by the sight or odor or even the thought of food. Mixed human saliva has usually a faintly alkaline reaction and always contains ptyalin (salivary amylase), although its amylolytic power appears to vary considerably with individuals and with the same individual at different times of the day. As the food comes in contact with saliva, the digestion of starch and dextrin under the influence of the ptyalin begins at once; but as mastication is an entirely voluntary act, the thoroughness with which the food becomes mixed with saliva is subject to wide variations.

Usually the food stays too short a time in the mouth for the starch to be acted upon there to any great extent, and until recently it was supposed that salivary digestion must cease almost as soon as the food reaches the stomach, since the activity of ptyalin is quickly checked by even small amounts of free hydrochloric acid. It was supposed that the food mass must soon be mixed with the gastric juice under the influence of the " churning " of the stomach contents by the muscular contraction of the stomach walls, which was so interestingly described by Dr. Beaumont in the account of his classical researches already referred to (pages 70–71). From the nature of the case Dr. Beaumont's observations were made entirely at one point in the stomach. Here he found during digestion a vigorous muscular churning and mixing of the food mass with the gastric juice. For a long time this was supposed to represent the state of the entire stomach contents. This view has now been abandoned as the result of a number of recent investigations, among which those of Cannon and of Grützner are of especial interest.

When a small amount of an inert metallic compound such as bismuth subnitrate is mixed with the food, it becomes possible to photograph the food-mass within the body by means of the Roentgen rays. By the use of this method Cannon has carried out an extended series of observations upon the movements of the stomach and intestines during digestion,[1] upon the results of which the statements concerning the mechanism of digestion in this chapter are chiefly based.

Cannon's observations, confirmed by those of other investigators, show that the vigorous muscular movements described by Beaumont, and which generally begin 20 to 30 minutes after the beginning of a meal, occur only in the middle and posterior, or pyloric, portion of the stomach, while the anterior portion, or fundus, which serves as a reservoir for the greater portion of the food, is not actively concerned in these movements and does not rapidly mix its contents with the gastric juice.

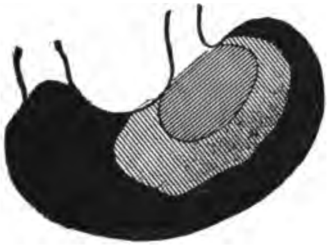

FIG. 5. — Section of frozen stomach of rat during digestion to show the stratification of food given at different times. (*Grützner.*) The food was given in three portions and colored differently. Reproduced from Howell's *Textbook of Physiology*, by permission of the W. B. Saunders Co.

That there is no general circulation and mixing of the entire stomach contents during or immediately following a meal is further shown by the experiments of Grützner, who fed rats with foods of different colors and on killing the animals and examining the stomach contents found that the portions which had been eaten successively were arranged in definite strata. The food which had been first eaten lay next to the walls of the stomach and filled the pyloric region, while the succeeding portions were arranged regularly in the interior in a concentric fashion (Fig. 5). In describing this result Howell says: "Such an arrangement of the food is more readily understood when one recalls that the stomach has never any empty space within; its cavity is only as large as its contents, so that the first portion of food eaten entirely fills it, and successive portions find the wall layer occupied and are therefore received into the interior."

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[1] These and other investigations are fully discussed in Cannon's *Mechanical Factors in Digestion*. See also Carlson's *Control of Hunger in Health and Disease.*

The character of the gastric juice secreted in different parts of the stomach varies considerably, especially as regards its acidity. In the middle region the secretion is rich in acid, while both in the cardiac region and at the extreme pyloric end, the " border cells " or " cover cells " (from which the secretion of the acid appears to take place) are few in number or entirely lacking, and the juice secreted in these regions may be neutral or, according to Howell, even slightly alkaline.

The nature and extent of the muscular movements also vary greatly in the different regions of the stomach. The peristaltic waves of muscular constriction which bring about the thorough mixing of the food with the gastric juice begin in the middle region and travel toward the pylorus. Over the pyloric part of the stomach when food is present constriction waves are continually coursing toward the pylorus. The food in this region is first pushed forward by the running wave and then by pressure of the stomach wall is returned through the ring of constriction. Thus the food *in this portion* of the stomach is thoroughly mixed with the gastric juice and is forced by an oscillating progress toward the pylorus.

The food in the cardiac end of the stomach is not moved by peristalsis, and so comes only slowly into contact with the gastric juice; and since the juice secreted here contains little if any free acid, a large part of the food mass remains for some time (variously estimated at from 30 minutes to 2 hours or more) in approximately the same neutral or faintly alkaline condition in which it was swallowed, and salivary digestion continues in this part of the stomach without interruption. Thus, if the food has been thoroughly chewed and well mixed with saliva before swallowing, much if not most of its starch may be converted into dextrin and maltose in the cardiac region of the stomach before the activity of the ptyalin is stopped by contact with the acid of the gastric juice.

The fundus, however, is not entirely inactive, but acts as a sort of elastic pouch which is distended by and slowly contracts upon the food mass, thus gradually tending to move the posterior portions and particularly the more fluid portion into the pyloric region. As digestion proceeds, the pylorus opens more frequently and the stomach tends to empty itself more and more freely, until finally the pylorus may open to allow the passage of particles which have not been acted upon by the gastric juice. Whether the stomach will thus completely empty itself of one meal before the eating of the next will depend of course upon the length of the interval and the amount and character of the food composing the meal. Small test meals may disappear in from 1 to 4 hours, but meals approximating one third of the day's food may not disappear entirely from the stomach during 6 or 7 hours.

In studying the passage of food from the stomach into the intestine, Cannon found that the pylorus does not open at the approach of each wave of constriction which passes over this part of the stomach, but only at irregular intervals. When the observations made by means of the Roentgen rays were supplemented by chemical examinations of stomach and intestinal contents removed at different stages, it appeared that the presence of free acid in the pyloric part of the stomach causes the pylorus to open, and its presence in the small intestine causes the pylorus to close. Thus it would appear that under normal conditions it is only when the protein of the food has become more or less completely saturated with hydrochloric acid and some of the latter remains in the free state, that the food is allowed to pass into the intestine.

Ordinarily, when each is fed separately, protein food stays longer in the stomach than carbohydrate, fat longer than protein, and mixtures of fat and protein leave the stomach more slowly than either alone. This is probably because fat tends to retard both the motility of the stomach and the secretion of the acid gastric juice. In general the softer or more fluid the fat the more rapidly it will leave the stomach; also emulsified fats tend to pass on more promptly than fat of the same kind taken in larger masses.

The difference noted between protein and carbohydrate is doubtless due to the fact that combination of the acid of the gastric juice with the protein of the food delays the appearance of free acid at the pylorus; for when protein food was acidulated before feeding and carbohydrate food was made alkaline, the protein was found to leave the stomach more rapidly than the carbohydrate. That the passage of food from stomach to intestine is governed mainly by the degree of acidity reached in the pyloric part of the stomach is of interest in view of the importance to the organism of the action of the acidity of the gastric juice in effecting a partial disinfection of the food. It has been found that when through any cause the hydrochloric acid of the gastric juice is abnormally decreased, the numbers of bacteria in the stomach contents may increase greatly. It will be seen also that the acidity of the chyme as it passes the pylorus has an important influence upon the secretion of the pancreatic juice.

The most important characteristics of gastric juice are the presence of free hydrochloric acid and of pepsin. While other acids may be found in stomach contents, the acidity of gastric juice appears to be due entirely to hydrochloric acid. Normal human gastric juice has been found by different observers to contain about 0.2 to 0.4 per cent of free hydrochloric acid.*

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* According to Carlson, "hunger juice" and "appetite juice" in man contain respectively 0.25 per cent and 0.40 per cent of free hydrochloric acid — averages of hundreds of observations upon a healthy man having a gastric fistula.

The stimuli which bring about secretion of gastric juice are both psychical and chemical.

Psychical stimulation results from the sensations of eating and may also be due to the sight and odor of food. The psychical secretion is studied chiefly by means of the "fictitious feeding" ("sham feeding") experiments in which food is given to dogs which have been prepared with esophageal openings through which the swallowed food escapes without entering the stomach. When such a dog is fed with meat, for example, there is a considerable secretion of gastric juice in spite of the fact that no food reaches the stomach. Such a flow of gastric juice is due to impulses received through the nervous system and specifically through the vagus nerve, for fictitious feeding has been found to cause a flow of gastric juice when the vagi are intact, but not after they have been cut. Secretion produced in this way reflexly as the result of the sensation of taste, odor, etc., is called by Pawlow a "psychic secretion" or "appetite juice." When the secretion is once started, even if no food enters the stomach, the flow of juice may continue for some time after the stimulus has ceased.

On the other hand, the normal secretion of gastric juice may be checked by unpleasant feelings such as fear, anger, or pain. This has been repeatedly observed with frightened or angry animals. Hornborg reports a similar observation upon a small boy. Food was shown but withheld, and the child became vexed and distressed, whereupon no gastric juice was secreted. After he was calmed, and given the food, it was some time before secretion began. Cannon infers, furthermore, that there is a "psychic tone" or "psychic contraction" of the gastro-intestinal muscles, analogous to the psychic secretion. In the same fashion that secretion may be checked, so also the movements of the stomach, bringing about the mixing of food with gastric juice and insuring its passage on into the duodenum, may be stopped during excitement or pain. This fact has been observed many times in experiments with various animals, as well as in the case of human beings.

If psychic secretion is normally excited, it insures the prompt beginning of gastric digestion. Stimulations arising within the stomach itself supplement the psychic influences and provide for the continued secretion of the gastric juice long after the mental effects of a meal have disappeared. This second stimulation is chemical and depends upon the production in the pyloric mucous membrane of a specific substance, or hormone, which acts as a chemical messenger to all parts of the stomach, being absorbed into the blood and thence exciting the activity of the various secreting cells of the gastric glands (Starling). Meat extracts, soups, etc., are particularly active in exciting the secretion which depends upon chemical stimulation; milk causes less secretion; white of egg is said to have no effect.

Under normal conditions, the amount of nutritive material absorbed from the stomach is insignificant as compared with the amount absorbed from the intestine. Nearly all the food eaten is passed from the stomach into the intestine in the form of chyme, having been more or less perfectly liquefied and acidulated by its thorough mixing with the gastric juice in the middle and pyloric regions of the stomach.

The stomach therefore has several functions. It serves (1) as a storage reservoir receiving food in relatively large quantities, say three times a day, and passing it on to the intestine in small portions at frequent intervals, (2) as a place for the continuation of the salivary digestion of starch, and (3) for the beginning of the digestion of proteins and perhaps fats, and finally (4) as a disinfecting station by virtue of the germicidal action of the hydrochloric acid of the gastric juice.

Intestinal Digestion

Digestion in the small intestine. — When the pylorus opens, food, now reduced to liquid chyme, is projected into the upper part of the small intestine, where it usually lies for some time in the curve of the duodenum, until several additions have been made to it from the stomach. While the food rests here the bile and pancreatic juice are poured out upon it, and here also, as well as in other parts of the small intestine, a certain amount of intestinal digestive juice ("succus entericus") is secreted by the glands of the lining membrane and mixed with the intestinal contents. While for purposes of description the pancreatic and intestinal juices and the bile may be discussed separately, it is to be remembered that in normal digestion they always act together. Cannon's observations showed that after a certain amount of food and digestive juices has accumulated as just described in the first loop of the small intestine, the mass all at once becomes segmented by constrictions of the intestinal walls, and the segmentation is repeated rhythmically for several minutes, so that the individual portions are subjected to relatively extensive and energetic to-and-fro movement, which is doubtless very important in facilitating the emulsification of fat. Other effects of the muscular constrictions which cause the segmentation are (1) a further mixing of food and digestive juices, (2) the bringing of the digested food into contact with the absorbing membrane, (3) the emptying of the venous and lymphatic radicles in the membrane, the material which they have absorbed being forced into the veins and lymph vessels by the compression of the intestinal wall. After a varying length of time the segmentation ceases and the small segments are carried forward individually by the peristaltic movement, or join and move on as a single body.

The fluid food mass which the stomach pours into the duodenum contains a small amount of free hydrochloric acid besides a larger amount combined with protein and sometimes organic acids from the food as eaten, or from bacterial fermentation of carbohydrates in the stomach. The pylorus having closed, the alkalinity of the bile, the pancreatic juice, and the intestinal juice combine to neutralize the acids present.

In man the main duct of the pancreas and the bile duct unite and empty into the small intestine about 8 to 10 cm. (3 to 4 inches) below the pylorus. *The pancreatic juice* is a clear liquid having an alkalinity probably equivalent to a 0.5 per cent solution of sodium carbonate and containing three important enzymes or their zymogens — trypsin, amylopsin (amylase), and steapsin or lipase.

The outflow of the pancreatic juice begins at once when any of the acid stomach contents passes through the pylorus, and has been shown by Bayliss and Starling to be due to a definite chemical substance, *secretin*, a typical hormone produced as the result of the action of the acid upon some constituent of the intestinal mucous membrane, which is absorbed and carried by the blood to the pancreas and there stimulates the flow of pancreatic juice.

Human bile, which, as already stated, enters the intestine through the same duct with the pancreatic juice, is a slightly alkaline solution containing, in addition to water and salts, bile pigments, bile acids (as salts), cholesterin, lecithin, and a peculiar protein derived from the mucous membrane of the bile ducts and gall bladder. The presence of the bile in the intestinal contents greatly increases the solubility of the fatty acids, while at the same time it diminishes the surface tension between watery and oily fluids. Bile may also accelerate the action of pancreatic lipase in a more direct way. Thus bile aids both the digestion and the absorption of fats. The bile acids are themselves absorbed to a considerable extent and again secreted by the liver. The secretion of bile by the liver, although variable in amount, is continuous. Its ejection from the gall bladder into the intestine occurs, however, only during digestion, and appears to be excited by the passage of chyme through the pylorus, and to run parallel to the outpouring of the pancreatic juice. According to Starling, the rapid flow of bile during intestinal digestion is due not only to the pouring out of what was previously stored in the gall bladder, but also to an increased rate of secretion to which the liver is stimulated by the same chemical mechanism which stimulates the flow of pancreatic juice.

The intestinal juice is a distinctly alkaline liquid secreted by the tubular glands (crypts of Lieberkühn) with which the small intestine is lined. It contains at least five enzymes: enterokinase, by the action of which trypsinogen is converted into trypsin, erepsin, which produces further cleavage of the proteoses and peptones; and the three enzymes, sucrase (or invertase), maltase, and lactase, which hydrolyze respectively the three disaccharides, sucrose, maltose, and lactose. The secretion of intestinal juice is probably stimulated by secretin, and possibly also by another hormone whose production is dependent upon the presence of pancreatic juice.

Careful observations on the reaction of the contents of the small intestine were made by Moore and Bergin in 1897.* Samples taken through a fistula immediately above the ileocæcal valve were always alkaline to methyl-orange, lacmoid, and litmus, but acid to phenolphthalein. Hence neither hydrochloric acid, nor any appreciable amount of the stronger organic acids such as acetic, butyric, or lactic, could have been present in the free state. The acid reaction shown by phenolphthalein was probably due either to traces of organic acids, or possibly to dissolved carbonic acid, or to acid-protein compounds not yet completely digested and absorbed. It seems probable that this fairly represents the condition as to reaction which exists throughout the greater part of the small intestine. Under such conditions all three classes of foodstuffs would be readily attacked by the digestive enzymes present, and brought into condition for absorption — the carbohydrates as monosaccharide; the fats as fatty acid and glycerol; the proteins (chiefly at least) as amino acids.

The rate of passage of different foodstuffs through the small intestine has been studied by Cannon with the aid of the Roentgen rays, according to the general method already described. Fat, carbohydrate, and protein foods, uniform in consistency and in amount (25 cc.), were fed to cats which had been fasted for 24 hours. At regular intervals for 7 hours after feeding, the shadows of the stomach and intestinal contents were observed by means of the Roentgen rays.

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* Very recently the subject has been reinvestigated by Long and Fenger, using modern methods for the actual measurement of hydrogen ion concentration. See *Journal of the American Chemical Society*, June, 1917.

The process of rhythmic segmentation above described was seen with all three kinds of foodstuffs, and the frequency of its occurrence corresponded roughly to the amount of food present in the intestine.

Absorption takes place very readily in the small intestine — more readily and completely than can be explained by the purely mechanical laws of diffusion. On this account the process is sometimes called " resorption " to distinguish it from passive absorption such as takes place by diffusion through non-living membrane.

Observations have been made upon a patient having a fistula at the end of the small intestine. In this case it was found that 85 per cent of the protein matter of the food was absorbed before this point was reached, and the absorption of the other foodstuffs is probably equally complete. For this patient the food began to pass the ileocæcal valve in from 2 to 5½ hours after eating, but the time required from the eating of the food until the last portions had passed into the large intestine was 9 to 23 hours.

Digestion in the large intestine. — We have seen that in the small intestine the conditions are very favorable both for digestion and for absorption, and that very much the greater part of the available nutrients has been absorbed before the food mass reaches the ileocæcal valve. Hertz has observed, however, that often the ileum is still full at the end of four or five hours after the last trace of chyme has left the stomach. Consequently there may be an accumulation of incompletely digested food and active digestive enzymes in the last few inches of the ileum, where it remains and undergoes digestion for perhaps a longer period than in the stomach. During all this time there is active segmentation, but very little peristalsis.

Beginning at infrequent intervals some time after the chyme first reaches it, the ileocæcal valve relaxes each time a peristaltic wave passes along the last few inches of the ileum. Cannon finds that the ileocæcal valve is physiologically "competent" for food which passes through it normally from the small intestine. This means that the food which has reached the large intestine in the natural way is ordinarily never forced back into the small intestine again. This is important because in the anterior portion of the large intestine the waves which appear most frequently are those of antiperistalsis — *i.e.* tend to force the food back toward the small intestine. Since the ileocæcal valve prevents the food passing back, these antiperistaltic waves result in thoroughly churning the food in this part of the large intestine and constantly bringing fresh portions in contact with the intestinal wall so that the conditions here are quite favorable for absorption. Moreover, the walls of the large intestine furnish an alkaline secretion which further aids the completion of the digestive changes already begun. So far as known the large intestine secretes no digestive enzyme of its own.

With the passage of material from the ileum into the cæcum, the cæcum and ascending colon become gradually filled. Recent observations show that this passive filling takes place very slowly except during and immediately after meals (Hertz). The material remains in the large intestine for a comparatively long time (generally about a day, often longer); for the peristaltic movements which carry the material onward, while stronger than the waves of antiperistalsis, are of less frequent occurrence, at least in the first part of the large intestine. During this time there is a marked absorption of water, along with the remaining products of digestion. The residual material gradually becomes more solid and takes on the character of feces.

Bacterial Action in the Digestive Tract

The digestive tract of an infant contains no bacteria at birth, but usually some gain access during the first day of life. In the average adult it is estimated that each day's food in its passage through the digestive tract is subjected to the action of over one hundred billion bacteria, chiefly in the large intestine.

Since bacteria are regularly present in the digestive tract in such large numbers, it has been questioned whether they may not perform some essential function in connection with the normal processes of digestion. Experiments to demonstrate whether animals are independent of such bacteria are beset with many difficulties. Nuttall and Thierfelder kept sterile for several days the digestive tracts of young guinea pigs delivered by Cæsarean section and fed upon thoroughly sterilized food, and as the animals thus treated lived and gained in weight, the experimenters concluded that intestinal bacteria are not essential to normal nutrition. This view has recently received strong support from the observations of Levin, who examined the intestinal contents of Arctic animals in Spitzenberg. The digestive tracts of white bears, seals, reindeer, eider ducks, and penguin were found to be in most cases free from bacteria, showing that the latter are not essential to the normal processes of digestion and nutrition. Kendall, however, in citing the evidence presented by Levin, points out that Arctic mammals, as soon as they are brought to temperate regions, rapidly acquire intestinal bacteria which do not seem to interfere with the well-being of the host.

Furthermore Schottelius claims that the conclusions of Nuttall and Thierfelder are not justified since their experiments did not cover a long enough period. He himself experimented with chickens from bacteria-free eggs. One group kept in an absolutely bacteria-free environment and fed on sterile food, did well for ten days, but thereafter developed very slowly. When they were given " infected " food (containing common bacteria), they gained rapidly. Meanwhile a second group which had been kept in a sterile environment but had received " infected " food from the start, grew normally, as did a third group kept throughout under ordinary conditions. From these results Schottelius concluded that intestinal flora seem to be necessary for the normal development of chickens. Similar observations have been made by Madame Metschinikoff using tadpoles, and by Moro using turtles.

Notwithstanding this conflicting evidence, it would seem fair to conclude from the observations of Levin that if it were possible to exclude absolutely all bacteria from the digestive tract, the well-being of the body would be in no wise impaired; yet under such conditions as ordinarily exist, the bacteria which usually predominate in the digestive tract of the healthy man probably render an important service in helping to protect the body against occasional invasions of obnoxious species.

According to Herter, a few species, such as *B. lactis aërogenes*, *B. coli*, *B. bifidus*, have adapted themselves so well to the conditions existing in the human digestive tract that they are ordinarily not harmful to the host unless present in abnormally large numbers, and being able to hold their own against newcomers they may act beneficially in giving rise to conditions which check the development of other types of organisms, capable of doing injury, which under ordinary conditions man can hardly prevent from occasionally gaining ingress through food or drink.

" The presence in the colon of immense numbers of obligate micro-organisms of the *B. coli* type may be an important defense of the organism in the sense that they hinder the development of that putrefactive decomposition which, if prolonged, is so injurious to the organism as a whole. We have in this adaptation the most rational explanation of the meaning of the myriads of colon bacilli that inhabit the large intestine. This view is not inconsistent with the conception that under some conditions the colon bacilli multiply to such an extent as to prove harmful through the part they take in promoting fermentation and putrefaction."

Proteolytic enzymes formed by intestinal bacteria may assist in the digestion of food, and it is conceivable that bacteria may synthesize proteins or amino acids which may then be absorbed by the host, but the recent experiments of Osborne and Mendel seem to show that this cannot be an important factor in protein metabolism.

If for our present purpose we consider only the bacteria which are prominent in producing decomposition of foodstuffs in the digestive tract, and these only with reference to this one property, we may regard as the three main types: (1) the bacteria of fermentation, such for example as the lactic acid bacteria; (2) the putrefactive bacteria, such as the anaërobic *B. aërogenes capsulatus* (*B. welchii*); (3) bacteria of the *B. coli* type, showing some of the characters of both the fermentative and putrefactive organisms, but tending in general to antagonize the putrefactive anaërobes.

Among cases of excessive bacterial decomposition in the digestive tract the fermentation of carbohydrates with production of organic acids (and possibly also alcohol) is most likely to occur in the stomach, while the putrefaction of proteins occurs mainly in the large intestine. While it is true that in general the products of fermentation tend to restrict putrefaction, yet, since the two processes take place for the most part at such widely separated points of the digestive tract, there may be excessive fermentation and excessive putrefaction in the same individual at the same time. Among the conditions which favor excessive fermentation are: diminished tone and motility of the stomach, dilation, diminution or absence of free hydrochloric acid in the gastric juice, and excessive use of carbohydrate food — especially sucrose and glucose, which are more susceptible to fermentation in the stomach than are lactose, maltose and starch.

In the normal human stomach the conditions are quite unfavorable for the development of anaërobic putrefactive bacteria, not only because of the presence of air, but also because of the action of the gastric juice; and favorable conditions are not found in the anterior portion of the small intestine. In the lower third of the small intestine the numbers of bacteria increase and among them sometimes putrefactive forms. In the large intestine the conditions are much more favorable for the anaërobic putrefactive bacteria, and these may produce marked decomposition in any protein still remaining unabsorbed. In general the greater the amount of digestible but undigested or unabsorbed protein and the longer the material stays in the large intestine, the greater the amount of putrefactive decomposition. Not infrequently excessive fermentation in the stomach causes local sensitiveness which results in the taking of less bulky food (or such as has less indigestible residue), which in turn tends to stagnate in the intestine and thus render the conditions more favorable for intestinal putrefaction. According to Herter there sometimes results from the eating of large quantities of meat and sugar a type of fermentation in which oxalic acid is produced and which must therefore be highly injurious; but ordinarily the products of fermentation are only irritating, while putrefaction gives rise to products which are more distinctly toxic. These include indol, skatol, phenol, and cresol, which are for the most part absorbed into the system and finally excreted in combination with sulphuric acid as " ethereal " or " conjugated " sulphates. Of these the best-known is potassium indoxyl sulphate, commonly called " indican." The amounts of conjugated sulphates and of indican in the urine are valuable indications of the intensity of the putrefactive process in the intestine.

Coefficients of Digestibility of Food

The fecal matter passed per day varies considerably in health, but, on an ordinary mixed diet of digestible food materials, is usually between 100 and 200 grams of moist substance containing 25 to 50 grams of solids. The feces contain any indigestible substances swallowed with the food and any undigested residues of true food material; but ordinarily they appear to be largely composed of residues of the digestive juices, together with certain substances which have been formed in metabolism and excreted by way of the intestine, and bacteria, living and dead.

Prausnitz studied the feces of several persons placed alternately on meat and on rice diets and found that, although the solids of the meat were about ten times as rich in nitrogen as the solids of the rice, the two diets yielded feces whose solids were of practically the same composition. Some of the data of these experiments are shown in the table.

COMPOSITION OF FECES FROM DIFFERENT DIETS (PRAUSNITZ)

PERSON	PRINCIPAL FOOD	NITROGEN IN DRY FECES PER CENT	ETHER EXTRACT IN DRY FECES PER CENT	ASH IN DRY FECES PER CENT
H. . . .	Rice	8.83	12.43	15.37
H. . . .	Meat	8.75	15.96	14.74
M. . . .	Rice	8.37	18.23	11.05
M. . . .	Meat	9.16	16.04	12.22
W. P. . .	Rice	8.59	15.89	12.58
W. P. . .	Meat	8.48	17.52	13.13

In view of such results Prausnitz considers that "normal" feces have essentially the same composition irrespective of the food, the quantity of food residues in such "normal" feces being negligible. From this point of view the feces show not so much the extent to which the food has been absorbed as whether it is a large or a small feces-former. On the other hand, so far as the nitrogen compounds of the feces are concerned, it is probably true, as generally assumed, that they represent material either lost or expended in the work of digestion, and therefore that the nitrogen of the feces is to be deducted from that of the food in estimating the amount available for actual tissue metabolism. This, however, is by no means equally true of the ash constituents, many of which after being metabolized in the body are eliminated mainly by way of the intestine rather than through the kidneys.

On a liberal diet consisting entirely of non-nitrogenous food the amount of nitrogen in the feces was 0.5 to 0.9 gram per day, which is more than is sometimes found in feces from food furnishing enough protein to meet all the needs of the body. Thus the expenditure of nitrogenous material in the digestion of fats and carbohydrates may be larger than in the digestion of protein food.

The feces always contain fat (or at least substances soluble in ether) as well as protein. Fasting men have eliminated 0.57 to 1.3 grams of "fat" per day; and when the diet is very poor in fat, the feces may contain as much as was contained in the food. As the fat content of the food rises, the actual amounts in the feces increase, but the relative amounts decrease, so that up to a certain point the apparent percentage utilization of the fat becomes higher. The limit to the amount of fat which can be thus well digested varies with the individual and with the form in which the fat is given. Quantities up to 200 grams per day have been absorbed to within 2 to 3 per cent when given in the form of milk, cheese, or butter.

In addition to protein and fat the feces always contain various other forms of organic matter which in the routine proximate analyses usually made in connection with feeding experiments are collectively reported as "carbohydrates determined by difference."

With these facts in mind one may make use of the coefficients of digestibility without being misled by them. These coefficients show the relation between the constituents of the food consumed and the corresponding constituents of the feces. Thus if the feces from a given diet contain 5 per cent as much protein as was contained in the food, this proportion is assumed to have been lost or expended in digestion, and the coefficient of digestibility of the protein of the diet is stated to be 95 per cent. While as just shown this assumption is not entirely correct, yet it is approximately true of the organic nutriments that the difference between the amounts in the food and in the feces represents what is available to the tissues of the body, and thus these coefficients serve a useful purpose in the computation of the nutritive values of foods.

From the results of hundreds of digestion experiments Atwater computed the coefficients of digestibility of the organic nutrients of the main groups of food materials, when used by man as part of a mixed diet, to be as follows: —

AVERAGE COEFFICIENTS OF DIGESTIBILITY OF FOODS WHEN USED IN MIXED DIET (ATWATER)

	PROTEIN PER CENT	FAT PER CENT	CARBOHYDRATES PER CENT
Animal foods	97	95	98
Cereals and breadstuffs .	85	90	98
Dried legumes	78	90	97
Vegetables	83	90	95
Fruits	85	90	90
Total food of average mixed diet	92	95	98

In some cases these figures are higher than have been reported for similar foods by other observers, the differences being due mainly to the fact (not formerly recognized) that a food may be more perfectly utilized when fed as part of a simple mixed diet than when fed alone. Milk is an example of such a food, and has when consumed as part of a mixed diet a much higher coefficient of digestibility than is often assigned to it on the basis of earlier experiments.

It will be seen that the coefficients differ less for the different types of food than might be expected from popular impressions of "digestibility" and "indigestibility." It is also noteworthy that the coefficients of digestibility are less influenced by the conditions under which the food is eaten and vary less with individuals than is generally supposed. In explanation of this it may be noted that general impressions of digestibility relate mainly to *ease* of digestion and particularly to ease and rapidity of gastric digestion, and that there is little direct relation between the ease with which a food is digested in the stomach and the extent to which it is ultimately digested in its passage through the entire digestive tract. Substances which are resistant to gastric digestion will tend to remain long in the stomach and will probably excite a greater flow of gastric juice. Thus a greater amount of acid chyme will enter the duodenum, and this will result in the secretion of a greater amount of pancreatic juice also.

Similarly an increase in the amount of food eaten may have little effect upon the coefficient of digestibility of the foodstuffs. In a series of experiments by the writer it was found that the doubling of a small diet decreased the coefficient of digestibility by less than 1 per cent. Snyder reports that as between medium and large amounts of oatmeal and milk, the protein was 7 per cent and the fat 6 per cent more completely absorbed in the case of the medium ration.

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CHAPTER V

THE FATE OF THE FOODSTUFFS IN METABOLISM

CARBOHYDRATES

THE carbohydrate of the food, having been converted into monosaccharides in the intestine, is taken up by the capillary blood vessels of the intestinal wall and passes from them into the portal vein. After a meal rich in carbohydrate the blood of the portal vein is rich in glucose, sometimes reaching twice its normal glucose content; and may show levulose and galactose as well. In the blood of the general circulation, however, only glucose is found, and this remains small in quantity — about one tenth of one per cent — even after a meal rich in carbohydrates, so that a considerable part of the carbohydrate taken must be stored temporarily in the liver and given up gradually to the blood in the form of glucose, thus keeping nearly constant the glucose content of the blood of the general circulation. The carbohydrate thus stored in the liver cells is deposited in the form of glycogen, which, after an abundant meal, may reach 10 per cent of the weight of the liver (or, in rare cases, an even higher figure) and may fall to nearly nothing when no carbohydrate food has been taken for some time. To a less extent the muscles store glycogen in a similar way, their glycogen contents varying from traces to about 2 per cent.

The fact that the carbohydrate stored in the liver after a meal is so largely converted into glucose and passes into the blood current before the next meal, while the glucose content of the blood remains small and nearly constant, indicates that the glucose of the blood must be quite rapidly used, and from our present standpoint the most important question of the carbohydrate metabolism is the fate of the glucose carried to the muscles and other tissues by the blood.

Oxidation of Carbohydrate

By comparison of the arterial and venous blood, it is plain that in its passage through the muscles the blood becomes poorer in glucose and oxygen and richer in carbon dioxide, and this change is more marked when the muscle is active than when it is at rest. The oxidation of glucose in the muscles is in some way dependent upon the pancreas, but the exact function of the pancreas in this connection is still obscure. It is not to be supposed that the glucose is burned directly to carbon dioxide and water. There is much evidence that the glucose molecule is broken before oxidation, and in all probability this first cleavage yields mainly three-carbon compounds.

Some lactic acid is always produced by working muscle and this has long been regarded as a possible intermediate product in the metabolism of glucose.* Lactic acid appears to bear important relationships both to carbohydrate metabolism and to muscle contraction. The discussion of the significance and rôle of lactic acid cannot be attempted here. It may be said, however, that in recent years much experimental evidence has accumulated in support of the view that lactic acid is not formed directly from glucose, but rather through the intervention of other three-carbon compounds, probably glyceric aldehyde or methyl glyoxal (pyruvic aldehyde) or both.

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* It should perhaps be noted here that lactic acid plays a part not only in the metabolism of carbohydrate but of other foodstuffs as well. It may be formed, for instance, from glycerol and from certain amino acids.

If we think of the glucose molecule as first breaking into three-carbon molecules with a minimum of internal rearrangement, the most probable primary product would appear to be glyceric aldehyde, the formation of which might be represented crudely as follows:

$$\mathrm{CH_2OH \cdot CHOH \cdot CHO} \,\vdots\, \mathrm{H \cdot CHOH \cdot CHOH \cdot CHO}$$

Or, to write the reaction in a more usual form,

$$\underset{\text{Glucose}}{\mathrm{C_6H_{12}O_6}} \rightarrow 2\ \underset{\text{Glyceric aldehyde}}{\mathrm{CH_2OH \cdot CHOH \cdot CHO}}$$

It is also possible that the first product of cleavage of glucose may be pyruvic aldehyde or methyl glyoxal:

$$\underset{\text{Glucose}}{\mathrm{C_6H_{12}O_6}} \rightarrow 2\ \underset{\substack{\text{Methyl glyoxal} \\ \text{(Pyruvic aldehyde)}}}{\mathrm{CH_3 \cdot CO \cdot CHO}} + 2\mathrm{H_2O}$$

Both glyceric aldehyde and methyl glyoxal have been shown to result from the cleavage of glucose under the influence of alkali *in vitro* and there are doubtless enzymes in the tissues which catalyze one or both of these reactions with the result that glucose readily undergoes such cleavage as a preliminary to oxidation in the body.

Opinion is at present divided as to whether glyceric aldehyde or pyruvic aldehyde (methyl glyoxal) is to be regarded as the usual first step in glucose metabolism. In either case it is probable that the bulk of the carbohydrate material passes through the form of pyruvic aldehyde (methyl glyoxal) on its way to oxidation.

According as we assume the process to go on with or without the intermediary formation of glyceric aldehyde, the production of lactic acid from glucose in the body may be represented in either of the following ways:

$$\underset{\text{Glucose}}{\mathrm{C_6H_{12}O_6}} \rightarrow \underset{\text{Glyceric aldehyde}}{\mathrm{CH_2OH \cdot CHOH \cdot CHO}} \rightarrow \underset{\text{Pyruvic aldehyde}}{\mathrm{CH_3 \cdot CO \cdot CHO}}$$

$$\rightarrow \underset{\text{Lactic acid}}{\mathrm{CH_3 \cdot CHOH \cdot COOH}}$$

or

$$\underset{\text{Glucose}}{\mathrm{C_6H_{12}O_6}} \rightarrow \underset{\text{Pyruvic aldehyde}}{\mathrm{CH_3 \cdot CO \cdot CHO}} \rightarrow \underset{\text{Lactic acid}}{\mathrm{CH_3CHOH \cdot COOH}}$$

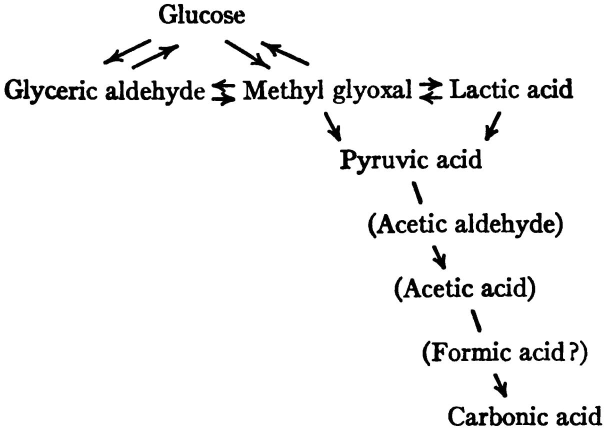
Each of these reactions has been brought about in the laboratory by heating with alkali and at the lower alkalinity of the body the tissue enzymes are believed to catalyze the same or similar changes. Moreover it has been shown that under suitable experimental conditions lactic acid is formed from glyceric aldehyde and from pyruvic aldehyde by the action of surviving liver tissue; and the further fact that in experimental diabetes glucose may be formed from glyceric or pyruvic aldehyde as well as from lactic acid tends also to confirm the belief that these aldehydes are intermediary products between glucose and lactic acid — both in normal metabolism and experimental diabetes. Glycerol also when perfused through liver tissue yields lactic acid, and since the first product of oxidation of glycerol is in all probability glyceric aldehyde, we have here a further reason for believing that the latter is a normal precursor of lactic acid. There has been no direct demonstration of the presence of glyceric aldehyde or of pyruvic aldehyde (methyl glyoxal) in the body; but this is probably due to their unstable or highly reactive nature. The view that glyceric aldehyde passes through pyruvic aldehyde in being transformed into lactic acid is not only probable on stereochemical grounds but is strongly supported by much recent evidence indicating that pyruvic aldehyde occupies a central position in the intermediary metabolism.

Thus far in our study of the catabolism of glucose we have considered no oxidative changes but only the cleavages and transformations which, from the standpoint of the use of glucose as fuel, may be regarded as preliminary to oxidation. Probably the first *oxidation* product to be formed in glucose catabolism is pyruvic acid, $CH_3 \cdot CO \cdot COOH$. This may be formed by the oxidation either of pyruvic aldehyde or of lactic acid. The relation of the three substances may be represented thus:

$$\begin{tikzcd}
\underset{\text{Pyruvic aldehyde}}{CH_3 \cdot CO \cdot CHO} \arrow[rr, shift left] \arrow[dr] & & \underset{\text{Lactic acid}}{CH_3 \cdot CHOH \cdot COOH} \arrow[ll, shift left] \arrow[dl] \\
& \underset{\text{Pyruvic acid}}{CH_3 \cdot CO \cdot COOH} &
\end{tikzcd}$$

Pyruvic aldehyde and lactic acid are, so to speak, upon the same energy plane. Molecule for molecule they are of equal fuel value and either is readily convertible into the other. The conversion of pyruvic acid into lactic acid or pyruvic aldehyde probably takes place under certain conditions, but this involves reduction and so is not to be expected in the normal course of glucose oxidation. The fate of pyruvic acid under normal conditions is probably to undergo further oxidation through acetic acid to carbonic acid and water. It is possible that acetaldehyde or alcohol or both may intervene between pyruvic acid and acetic acid, and that formic acid may be produced as an intermediate step between acetic and carbonic acids.

To summarize what now appears to be the most promising theory of the intermediary metabolism of carbohydrate, we may say that the glucose is first transformed, either directly or through glyceric aldehyde, into pyruvic aldehyde (methyl glyoxal), which may either be changed to lactic acid or oxidized directly to pyruvic acid that readily undergoes oxidation to carbon dioxide and water through steps not yet fully worked out. Lactic acid may also be converted into pyruvic acid and thus ultimately be completely oxidized. In case of excessive formation or inadequate oxidation, as in extreme muscular fatigue or asphyxial conditions, lactic acid may accumulate in the body or may be excreted unchanged.



Whatever the exact mechanism of the process, a large part of the glucose brought by the blood is oxidized in the muscles to furnish energy, which appears as external or internal work.

In general, the rate at which combustion takes place in the tissues depends upon the activity of the tissue cells, rather than upon the supply either of combustible matter or of oxygen. When a sufficient supply of oxygen is provided, any further increase has little effect upon the rate of combustion, and, as we have seen, any excess of carbohydrate instead of being burned is stored as glycogen. But while the absorption of an abundance of carbohydrate does not greatly change the amount of combustion taking place in the body, it may result in the use of carbohydrate as fuel almost to the exclusion of fat for the time being, as is shown by observations upon the respiratory quotient.

The respiratory quotient is the quotient obtained by dividing the volume of carbon dioxide given off in respiration by the volume of oxygen consumed. That is —

$$\frac{\text{Volume of } CO_2 \text{ produced}}{\text{Volume of } O_2 \text{ consumed}} = \text{“ Respiratory quotient.”}$$

The numerical value of this quotient will evidently depend upon the elementary composition of the materials burned. Carbohydrates will yield a quotient of 1.0 since they contain hydrogen and oxygen in proportions to form water, so that all oxygen used to burn carbohydrate goes to the making of carbon dioxide, and each molecule of O_2 so consumed will yield one molecule of CO_2, occupying (under the same conditions of temperature and pressure) the same amount of space as the oxygen consumed to produce it. Thus in burning a molecule of glucose, six molecules of oxygen are consumed and six molecules of carbon dioxide produced:

$$C_6H_{12}O_6 + 6\,O_2 \rightarrow 6\,CO_2 + 6\,H_2O.$$

Here the volumes of oxygen and of carbon dioxide are equal and the respiratory quotient is 1.0.

Fats contain much more hydrogen than can be oxidized by the oxygen present in the molecule, and therefore a part of the oxygen used to burn fat goes to form water, so that the volume of oxygen consumed is greater than the volume of carbon dioxide produced, which gives a respiratory quotient lower than 1.0. The common fats of the body and of the food give quotients approximating 0.7. Thus the oxidation of stearin is represented by the equation:

$$2\,C_{57}H_{110}O_6 + 163\,O_2 \rightarrow 114\,CO_2 + 110\,H_2O.$$

Since 163 volumes of oxygen are consumed and 114 volumes of carbon dioxide produced, the respiratory quotient is

$$\frac{114}{163} = 0.699.$$

Proteins give quotients intermediate between those of carbohydrates and fats, but if the amount of protein used in the body be determined by other methods (see Chapter VIII) and allowed for, one may then deduce from the respiratory quotient the proportions of carbohydrates and fats which are being burned in the body at any given time. The body will show a respiratory quotient of 1.0 when burning carbohydrate alone, of 0.7 when burning fat alone, and of an intermediate value when both fat and carbohydrate are being burned. If, now, the respiratory quotient rises soon after the eating of carbohydrate food, it is evident that the carbohydrate is being used more freely and fat less freely than before.

In an experiment by Magnus-Levy the subject before taking food showed a quotient of 0.77. He then ate 155 grams of cane sugar, after which the quotient was determined at intervals of an hour for 7 hours with the following results: 1.01, 0.89, 0.89, 0.92, 0.82, 0.82, 0.79. The quotient here shows that within an hour after the sugar was eaten the body was making use of the carbohydrate to such an extent that fat either was not being used at all or was being formed from carbohydrate as fast as it was burned; and that for seven hours after the meal the body continued to use carbohydrate to a greater, and fat to a less, extent than was the case at the beginning of the experiment.

It has been pointed out that, when carbohydrate is absorbed in larger quantity than is required to meet the body's immediate needs for fuel, the surplus normally accumulates as glycogen, which is stored conspicuously in the liver, but also to a considerable extent in the muscles and other organs. The amount of carbohydrate which will be stored in the entire body after rest and liberal feeding is estimated at 300 to 400 grams. Thus the total amount of carbohydrate which can be stored as such in the body is no more than is frequently taken in one day's food.

When the supply of carbohydrate is so abundant that it continues in excess of the needs of the body and accumulates until the liver and muscles have no tendency to increase their store of glycogen, the further surplus of carbohydrate tends to be converted into fat.

Production of Fat from Carbohydrate

Experimental evidence of the transformation of carbohydrate into fat has been cited in Chapter II where it was shown that animals which fatten readily on carbohydrate food may store more body fat than could possibly be derived from the fats and proteins eaten; that milch cows have yielded more fat in the milk than could be accounted for on any other assumption than that fat was formed from carbohydrate; and that there may be more carbon stored in the body from the carbohydrate food eaten by a fattening animal than can be accounted for in any other way than that a part of the carbon taken into the body as carbohydrate was retained as body fat.

Further proof of the ability of the animal body to change carbohydrate into fat is obtained from the respiratory quotient. As noted above, observations made after a fast tend to show quotients approaching that of fat, while after feeding carbohydrates the quotient may rise rapidly. If the quotient reaches 1.0, it shows that the body as a whole is using carbohydrate and not fat as fuel; and a quotient greater than 1.0 may be taken as evidence that the carbohydrate is itself supplying part of the oxygen which appears as carbon dioxide, or, in other words, that it is breaking down in such a way that a part is burned while another part goes to form in the body a substance more highly carbonaceous and having a lower respiratory quotient than the carbohydrate itself. In many cases it is certain that this substance can be nothing but fat. Respiratory quotients greater than 1.0 have been observed after liberal carbohydrate feeding in several species, including man. Each such observation furnishes evidence of a conversion of carbohydrate into fat.

The formation of fat from carbohydrate in the animal body is therefore established by four distinct lines of experimental evidence: (1) by determination of the amounts of body fat formed, (2) by determination of the milk fat produced, (3) by observation of the amount of carbon stored, (4) by observations upon the respiratory quotient.

Chemical Steps in the Formation of Fat from Carbohydrate

While there is no doubt whatever of the ability of the animal to synthesize fat from carbohydrate, the mechanism of the process is far from clear. As expressed by Leathes, " the chemical changes involved are fascinating in their obscurity." Whatever the exact steps, the transformation of carbohydrate into fatty acid radicles must involve reduction of hydroxyl groups and condensations to form the long chains of the higher fatty acids. We have already seen that in what we believe to be the normal course of carbohydrate catabolism there occurs, either along with or quickly following the breaking of the glucose molecule into three-carbon compounds, a reduction of certain hydroxyl groups with transfer of the oxygen so that substances such as methyl glyoxal, pyruvic acid, and lactic acid are formed. From pyruvic acid or lactic acid acetaldehyde may be formed; two molecules of acetaldehyde may then undergo aldol condensation and the aldol be transformed (by simultaneous reduction and oxidation, or transfer of oxygen from the β to the terminal carbon) into butyric acid. Such an hypothesis is consistent with reactions observed *in vitro* and with the well-known production of butyric acid in certain bacterial fermentations of sugar and of lactic acid. Leathes favors this hypothesis and comments upon it (in part) as follows: " The biochemical significance of the synthesis of butyric acid from lactic acid and from sugar by bacteria becomes greater, however, when it is remembered that in this fermentation normal caproic acid is simultaneously formed, and as Raper showed also, though in still smaller amount, normal octoic or caprylic acid. . . . In butyric fermentation it seems that the reactions that lead to the synthesis of butyric acid may lead to the synthesis of acids of longer chains but still unbranched and containing an even number of carbon atoms, in other words, that these acids may be produced by condensation of two, three, or four acetic aldehyde molecules. In higher organisms, plants or animals, this same condensation carried further would result as Nencki suggested in the formation of the series of acids with straight chains of even numbers of carbon atoms leading up to palmitic and stearic acid." Raper[1] has shown experimentally that condensation of two molecules of aldol in alkaline solution yields a straight chain product which on oxidation and reduction by laboratory methods yields normal octoic (caprylic) acid.

Smedley has developed an alternative hypothesis regarding the mechanism of fatty acid synthesis from carbohydrate material.

According to Smedley,[2] the most probable starting point is pyruvic acid.

As an intermediary step in the metabolism of carbohydrate, pyruvic acid is probably formed in large quantities in the body, though its reactivity may prevent it from accumulating in measurable amounts.

Pyruvic acid readily breaks down to acetaldehyde and carbon dioxide. It also condenses with aldehydes to form products which, under conditions similar to those existing in the body, undergo rearrangements (through simultaneous or successive oxidation and reduction) which result in the splitting out of carbon dioxide leaving an acid of two more carbon atoms than were contained in the original aldehyde; or an aldehyde of two more carbon atoms than the original aldehyde may be formed, and this in turn react with another molecule of pyruvic acid forming a fatty acid or aldehyde of two more carbon atoms.

Each of these hypotheses assumes as a starting point only substances which we have good reason to believe are regularly formed in carbohydrate metabolism, and both are consistent with the well-known fact that natural fats contain fatty acid radicles having all multiples of two carbon atoms from four to eighteen, but none containing uneven numbers of carbon atoms in the molecule.

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[1] *J. Chem. Soc.*, Vol. 91, page 1831 (1907). See also Leathes, *The Fats*, pages 106–109.

[2] *Journal of Physiology*, Vol. 45, Proc. page 26; *Biochemical Journal*, Vol. 7, page 364.

FAT

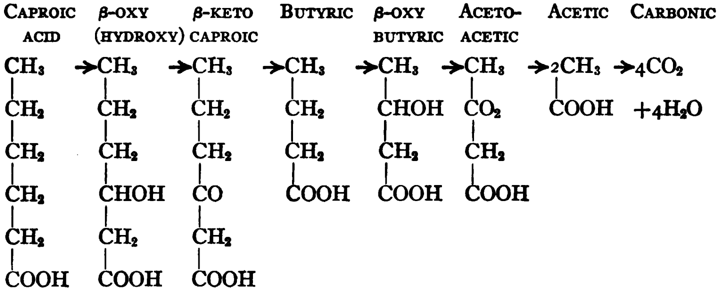
In digestion the fat is split into fatty acids and glycerol which, however, upon absorption are recombined into neutral fat. It is believed that this recombination occurs during the passage of these digestion products through the intestinal wall. The fat thus absorbed is taken up by the lymph vessels rather than the capillary blood vessels, and is poured with the lymph into the blood. The fat which renders the blood plasma turbid at the height of absorption will usually have passed from the blood into the tissues after a few hours. The fat thus leaving the blood may be burned as fuel, or stored for use as fuel in the future, and a part may be transformed into tissue lipoid or enter into combination with proteins to form some of the chemically more complex substances of cellular protoplasm, cell membrane, or of the central nervous system. The fat burned as fuel serves as a source of energy for muscular work and other activities essentially as does carbohydrate. The average results of a very complete series of experiments by Atwater and his associates indicated that the potential energy of fat was 95.5 per cent as efficient as that of carbohydrates for the production of muscular work.

Oxidation of Fat

The glycerol from fat is presumably oxidized to glyceric aldehyde which passes to methyl glyoxal, whose fate is doubtless the same in this case as when the same substance is formed in carbohydrate metabolism.

The fatty acid presents a separate problem. Through the work of Dakin, and of Knoop and Embden the "beta-oxidation theory" has been developed and is now generally accepted. According to this theory the fatty acid is attacked by oxidation at the β-carbon atom with the probable formation first of β-hydroxy, and then of β-ketonic acids. Further oxidation at this point must then cause a separation of the α- and β-carbon atoms; thus two carbons of the original fatty acid break away, presumably to undergo complete oxidation, and there remains a fatty acid with two less carbon atoms than the original. By such a process stearic acid would yield palmitic; palmitic would yield myristic; myristic, lauric; and so on to butyric acid. Beta-oxidation of butyric acid would yield successively β-oxybutyric, and acetoacetic acid. Normally the acetoacetic acid should yield two molecules of acetic, which in turn should burn to carbon dioxide and water.

The sequence of changes from caproic acid to the final oxidation products would thus be as follows:



$$\begin{array}{llllllll}
CH_3 & \rightarrow CH_3 & \rightarrow CH_3 & \rightarrow CH_3 & \rightarrow CH_3 & \rightarrow CH_3 & \rightarrow 2CH_3 & \rightarrow 4CO_2 \\
| & | & | & | & | & | & | & \\
CH_2 & CH_2 & CH_2 & CH_2 & CHOH & CO_2 & COOH & +4H_2O \\
| & | & | & | & | & | & & \\
CH_2 & CH_2 & CH_2 & CH_2 & CH_2 & CH_2 & & \\
| & | & | & | & | & | & & \\
CH_2 & CHOH & CO & COOH & COOH & COOH & & \\
| & | & | & & & & & \\
CH_2 & CH_2 & CH_2 & & & & & \\
| & | & | & & & & & \\
COOH & COOH & COOH & & & & &
\end{array}$$

When the normal process is interfered with or overtaxed, another reaction may occur with the formation from acetoacetic acid of carbon dioxide and acetone, which latter like acetoacetic acid and β-oxybutyric acid sometimes appears in the urine, especially in many cases of diabetes mellitus. The acidosis of diabetes is believed to be due to the β-oxybutyric acid and acetoacetic acid thus formed. Acetone, acetoacetic acid, and β-oxybutyric acid are sometimes spoken of collectively as "acetone bodies." For further discussion of the intermediary metabolism of fat and of the evidence that the acidosis of diabetes is chiefly due to acids arising from fat metabolism, the reader is referred to Dakin's *Oxidations and Reductions in the Animal Body* and the chapter on diabetes in Lusk's *Science of Nutrition*.

Storage of Food Fat in the Body

That fat derived from the food may be stored as body fat has already been shown (Chapter III) and need not be discussed further here. Recently Mills[1] has found that fatty oils injected with antiseptic precautions into the subcutaneous tissue may under favorable conditions be absorbed therefrom and used in the body in the same way as if obtained by feeding. Whether fat once deposited in the tissues will remain and accumulate, or be returned to the circulation and used as fuel, will depend upon the balance between the food consumption and the food requirements of the organism as a whole. In this respect, there is no difference between fat consumed and deposited as such and fat formed in the body from other food materials.

Can Carbohydrate be Formed from Fat?

Glycerol is readily convertible into glucose in the body, probably passing through the form of glyceric aldehyde as an intermediate step; but the glycerol radicle represents only about one twentieth of the energy value of the fat molecule.

Whether carbohydrate is ever formed from fatty acid in the animal body is an open question.

As evidence of such formation of carbohydrate from fat, Hill cites observations upon hibernating animals showing increase of glycogen during sleep, accompanied by respiratory quotients lower than 0.7.

[1] *Archives of Internal Medicine*, Vol. 7, page 694 (1911).

On the other hand, in phlorizin poisoning * and severe diabetes when it would seem that all material in the body capable of transformation into glucose is being thus changed, there does not appear to be a production of glucose from fat (fatty acid). As this latter type of experimentation has been extensively employed while relatively little evidence of the sort cited by Hill has been presented, the trend of opinion is rather away from the view that the animal body can form carbohydrate from fatty acid radicles, or transform fat into carbohydrate beyond the limited amount obtainable from the glyceryl radicles of the fat. It has been suggested that the low respiratory quotients above mentioned may be due to accidental fluctuations, since the blood does not always show the same carbon dioxide content. The question of actual transformation of fat into carbohydrate is not of great practical importance in normal nutrition, because under normal conditions fats may be used interchangeably with carbohydrates as source of energy to a very large, though not unlimited, extent.

PROTEINS

It is now believed that the hydrolysis of proteins to amino acids in the digestive tract is practically complete. The significance of this digestive cleavage lies not simply in the formation of more soluble and more readily diffusible substances, but also in the resolution of the complex molecules of food protein into their simple amino acid " building stones " (" Bausteine ") which may be rearranged by the body in the synthesis of its own tissue proteins.

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* Phlorizin causes very great glycosuria and, if the poisoning is continued, the usual symptoms of severe diabetes such as muscular weakness, acidosis, acetonuria, and death in coma. From moderate dosage, however, the animal recovers. The glucose content of the blood falls (instead of rising as in true diabetes). The action of the phlorizin appears to be primarily upon the kidneys, causing them to secrete glucose much more rapidly than usual, thus draining off the glucose from the blood and keeping it below the normal level.

Absorption and Distribution of Protein Digestion Products

The work of the past few years, to be described in the paragraphs which follow, indicates that the amino acids, resulting from digestive hydrolysis of the food proteins, pass through the intestinal wall and into the blood of the portal vein unchanged, are carried through the liver into the blood of the general circulation and are thus distributed throughout the body, and are rapidly absorbed from the blood into the various tissues. Thus each tissue receives its protein material in the form of amino acids from which can be synthesized the particular kind of protein characteristic of the tissue in question. In other words, each tissue makes its own proteins from the amino acids brought by the blood. Amino acids not used in synthesizing protein (whether brought by the blood or formed by breakdown of tissue material) are broken down or deaminized in the tissues in the manner described beyond.

A brief account of recent work on the distribution and immediate fate of the amino acids may serve to give a more adequate impression of the modern view.

In 1906 Howell obtained a qualitative reaction for amino acids in the blood, but conclusive evidence of the relation of these amino acids to metabolism required the development of better methods than were then available for the estimation of amino acid nitrogen in the fluids and tissues of the body. Such methods were developed and applied independently and almost simultaneously in 1912 by Folin and Denis and by Van Slyke and Meyer.

Folin and Denis distinguished between the nitrogen of proteins, non-proteins, ammonia, and urea. The non-protein nitrogen includes that of amino acids and they were able to show that this form of nitrogen increased in the blood and tissues when glycine or a mixture of amino acids resulting from pancreatic digestion of protein was undergoing absorption from the small intestine. Moreover the increase in the non-protein nitrogen of the blood and muscles was nearly sufficient to account for the nitrogenous material absorbed from the intestine, from which it appeared that they had traced the absorbed amino acids and found them to be carried through the blood and to the muscles without being either built up into protein or broken down into ammonia or urea on the way. Urea formation was found to follow distinctly later than the absorption and distribution of the amino acids.

Van Slyke and Meyer estimated amino acids by quantitative determination of the nitrogen present as amino groups in the non-protein fraction of the blood or tissue. They found that, during the digestion of protein, amino acids pass through the intestinal wall and appear not only in the portal blood but also in the blood of the general circulation, showing that the amino acids, for the most part at least, pass both the intestinal wall and the liver unchanged.

Closely following the work of Folin and of Van Slyke, Rona (1912) demonstrated by experiments upon isolated segments of intestine that the amino acids pass unchanged through the intestinal wall; Abel (1913) dialyzed free amino acids from the circulating blood of living animals by means of his vivi-diffusion apparatus and actually separated alanine in crystalline form; and Abderhalden (1914) separated glycine, alanine, valine, leucine, aspartic acid, glutamic acid, lysine, arginine, histidine, and tryptophane from large quantities of shed blood. Soon afterward (1915) Henriques and Andersen showed that dogs and goats could be kept in a normal condition of nutrition and might even store nitrogen and gain weight when they were nourished exclusively by intravenous injection of a food solution containing nitrogen only in the form of completely digested protein — a strong confirmation both of the completeness of cleavage of protein in normal digestion and of the fact that the body is nourished by free amino acids carried by the blood without intervention of chemical changes in the intestinal wall.

Van Slyke (working upon dogs) continued his investigation of the fate of the amino acids and found that they are rapidly taken up from the blood by the tissues where they seem to be held by adsorption. Since the amino acids can be extracted by means of cold water or alcohol they do not seem to be held in chemical combination with the tissue proteins nor can simple diffusion account for the extent to which they enter the tissues, because they rapidly attain a higher concentration in the muscle and liver cells than in the blood with which these are in contact. The extent to which this concentration of amino acids in the muscles may go seems to have a fairly definite limit at about 75 milligrams of amino acid nitrogen per 100 grams of muscle. In the case of liver tissue this "saturation capacity" seems somewhat more elastic and the concentration may reach about twice the maximum observed in muscle, *i.e.* up to 150 milligrams of amino acid nitrogen per 100 grams of liver. In the muscles the amino acids taken up as just described disappear only very gradually and may not seem to be appreciably changed for several hours; in the liver they disappear rapidly; in the kidney, pancreas, and spleen they disappear less rapidly than in the liver.

The disappearance of the amino acids from the tissues may be due either to a building up into protein or a breaking down with the formation of ammonia and urea or both. It seems probable that in general both processes go on in all tissues, each tissue building its own proteins and each also taking part in the deaminization of amino acids with formation of ammonia or urea. The more rapid disappearance of amino acids from the liver tissue is probably due to the greater activity of the liver in deaminization and urea formation, especially since Van Slyke has recently measured the increase of urea in the blood on its passage through the liver and shown that the passage of the blood through the muscle under parallel conditions does not increase its urea content to a measurable extent.

Van Slyke's experiments also show that the blood contains amino acids at all times and that the tissues are not freed from amino acids by fasting, while on the other hand high protein feeding does not result in any great accumulation of amino acids as such either in the blood or tissues. All these observations confirm the view that amino acids are the normal intermediary products in both the building up and breaking down of body protein and that any large storage of nitrogen in the body must be due to formation of body protein and not to mere accumulation of free amino acids.

Utilization of Protein in the Tissues

The proteins of the digested food, absorbed and distributed in the form of amino acids as described above, soon become available for nutrition; and among other functions they, like the carbohydrates and fats, may be burned * as fuel for muscular work. Pflüger proved that protein may serve as a source of muscular energy by feeding a dog for 7 months exclusively upon meat practically free from fat and carbohydrate, and requiring it throughout the experiment to do considerable amounts of work, the energy for which must in this particular case have been derived largely from the protein consumed.

The experimental facts and theoretical explanations regarding the breaking down of proteins (or of the amino acids arising from them) in the body tissues must now be considered. By experiment it has been found that if a meal extra rich in protein be eaten, an increased elimination of nitrogenous end products can be observed within 2 or 3 hours, and probably much the greater part of the surplus nitrogen will have been excreted within 24 hours of the time it was taken into the stomach. It does not follow, however, that the whole of the protein mole-

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* It will of course be understood that the protein is not supposed to be burned directly. Protein is split to amino acids, the amino acids deaminized, and the non-nitrogenous residues of the amino acids are burned.

cule is broken down and eliminated so quickly, and many experiments have shown that the carbon often does not leave the body so rapidly as does the nitrogen. Evidently, the nitrogenous radicles of the protein may be split off in such a way as to leave a non-nitrogenous residue in the body, and the study of protein metabolism involves a consideration of the fate of both the nitrogenous and the non-nitrogenous derivatives. The fate of the latter may conveniently be considered first on account of its relation to the metabolism of carbohydrates and fats. Of special interest is the problem to what extent the deaminized cleavage products of protein may be actually transformed into carbohydrate or fat in the body.

Formation of Carbohydrate from Protein

As early as 1876 Wolffberg tested the formation of carbohydrate from protein by fasting fowls for two days in order to free them from glycogen and then feeding for two days with meat powder which had been washed free from carbohydrate. Two of the fowls were killed soon after this protein feeding and showed more glycogen in their livers and muscles than could be accounted for except as derived from the protein fed. Two similar fowls killed 17 and 24 hours after feeding showed much less glycogen. This formation of glycogen from protein was fully confirmed by Kulz in a long series of experiments in which the food consisted of chopped meat thoroughly extracted with warm water (Lusk).

Independent evidence of the production of carbohydrates from protein is found in the work of Seegen, who chopped and mixed the liver of a freshly killed animal and determined the amount of carbohydrate in it by analysis of a portion, while the remainder was kept at body temperature and sampled for analysis from time to time. The percentage of carbohydrate was found to increase, showing that the liver cells can form carbohydrate from their own protein substance.

The most striking evidence of the origin of carbohydrate from protein in the animal body is found in the many observations and experiments which have been made in cases of diabetes, and in experimental glycosuria produced either by administration of phlorizin or by removal of the pancreas. In such cases large amounts of carbohydrate may be given off in the form of glucose even when there is little body fat and no carbohydrate or fat is fed. The glucose must therefore result from the metabolism of protein. In Lusk's exhaustive experiments upon dogs rendered diabetic by phlorizin, 58 per cent of the total weight of protein broken down in the body (whether in fasting or on a meat diet) was eliminated in the form of glucose. According to Lusk: "After ingestion of protein in the normal organism this sugar becomes early available and may be burned before the nitrogen belonging to it is eliminated, or, if the sugar be formed in excess, it may be stored as glycogen in the liver and muscles for subsequent use. In this way it is obvious that at least half the energy in protein may be independent of the curve of nitrogen elimination, but may rather act as though it had been ingested in the form of carbohydrates."

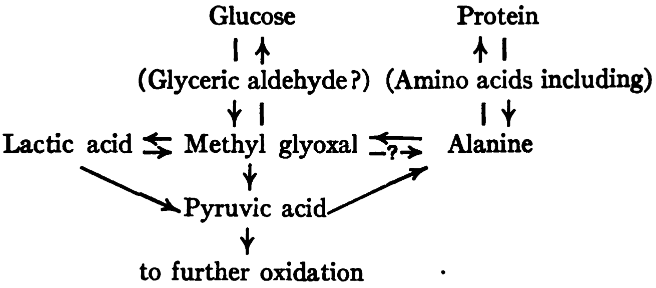
The way in which the production of carbohydrate from protein may take place has received much attention. Lusk demonstrated experimentally that alanine, one of the cleavage products of all known proteins, may yield glucose abundantly in the body; and he suggested that the change might occur through the formation of lactic acid as an intermediary product, since he had already shown that lactic acid is convertible into glucose. The work of Dakin has thrown further light on the intermediate steps of this transformation. He has shown that glyoxals have been formed from α-amino and α-hydroxy acids, *in vitro* — *e.g.* pyruvic aldehyde (methyl glyoxal) from alanine and lactic acid; and on the other hand α-hydroxy acids have been formed from glyoxals, both *in vivo* and *in vitro*.

$$\underset{\text{Alanine}}{CH_3\text{—}CHNH_2\text{—}COOH} \rightarrow \underset{\text{Methyl glyoxal}}{CH_3\text{—}CO\text{—}CHO} + NH_3$$

$$\underset{\text{Lactic acid}}{CH_3\text{—}CHOH\text{—}COOH} \rightleftarrows \underset{\text{Methyl glyoxal}}{CH_3\text{—}CO\text{—}CHO} + H_2O$$

Attempts, however, to synthesize amino acids directly from glyoxals *in vitro* were not successful. There is some evidence of that synthesis *in vivo*, but it cannot be considered as fully established whether it takes place directly by the addition of ammonia to free glyoxals, or whether the α-amino acid is formed secondarily from the α-ketonic acid, resulting from the oxidation of glyoxals. The work of Knoop and of Embden and Schmitz leaves no doubt of the ability of the liver cells to form amino acids from the ammonium salts of the corresponding α-ketonic acids. Alanine, phenylalanine, and tyrosine were produced in this way.* It is of course possible that there may have occurred, in these liver perfusion experiments, intermediate steps not recognized by the investigators, but this does not detract from the significance of the fact that the synthesis of amino acids from ammonium salts has now been repeatedly demonstrated by experiment.

The relations emphasized by Dakin may be represented as follows:



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* Embden also obtained alanine after perfusion of ammonium lactate, but the lactate may have been first changed to pyruvate and the alanine formed from the latter.

Attention may be called in passing to the possible importance of the interrelations of alanine, methyl glyoxal, and lactic acid to the regulation of neutrality, not only in the body as a whole (Chapter IX) but also in the particular cells in which deamination may be more active than oxidation. It will be noted that alanine (a nearly neutral substance) yields on deamination another neutral substance (methyl glyoxal) and a base (ammonia)

$$CH_3—CHNH_2—COOH \rightarrow CH_3—CO—CHO + NH_3$$

And furthermore that the neutral substance methyl glyoxal may react with water to form lactic acid

$$CH_3—CO—CHO + H_2O \rightarrow CH_3—CHOH—COOH$$

Experiments *in vitro* have shown that the production of lactic acid from methyl glyoxal is promptly checked unless the free acid is quickly neutralized; also that the conversion of alanine into methyl glyoxal and ammonia is accelerated by acids (Dakin).

Thus far the possible mechanism of formation of carbohydrate from protein cleavage products has been considered here chiefly in terms of alanine. To what extent is its behavior representative of that of the other amino acids? Experiments *in vitro* show that the transformation of an α-amino acid into the corresponding α-ketonic aldehyde is a very general reaction. Dakin and Dudley demonstrated it for all the amino acids with which they worked — glycine, alanine, phenylalanine, valine, leucine, and aspartic acid. Experiments *in vivo* (chiefly on dogs rendered diabetic by phlorizin poisoning) have shown that glycine, alanine, serine, cystine, aspartic acid, glutamic acid, arginine, and proline are all capable of yielding large amounts of glucose. Leucine, tyrosine, and phenylalanine when similarly administered to phlorizinized dogs increase the elimination of acetoacetic acid rather than glucose. Valine, lysine, and tryptophane yield neither glucose nor acetoacetic acid to any important extent (Dakin).

The amino acids which yield glucose are called glucogenetic, and the amount of glucose which a given protein can yield in the body will naturally depend upon the glucogenetic amino acid radicles which it contains. Since the amino acids resulting from protein hydrolysis cannot be quantitatively recovered by any laboratory method thus far developed, it is not yet possible to calculate just how much carbohydrate a given protein should theoretically yield. For meat protein and some others the yield has been determined experimentally as in Lusk's investigations cited above. For further discussion of this point see Lusk's *Science of Nutrition.*

We have therefore abundant evidence from the work of independent investigators, using different methods, that the animal body may form carbohydrates readily and in large proportion from the protein of the food; and the mechanism of the process is beginning to be fairly well understood.

Production of Fat from Protein

There has been much controversy regarding the formation of fat from protein in the animal body. A number of observations by Voit which were believed to demonstrate such a production of fat were subjected to vigorous criticism by Pflüger and apparently shown to be capable of other interpretations. Later experiments by Cremer in Voit's laboratory appear, however, to establish the formation of body fat from protein food beyond reasonable doubt.

Thus in one of these experiments a cat after a preliminary period of fasting was placed in a respiration apparatus and fed liberally with lean meat for eight days. The amount of protein broken down in the body was estimated from the nitrogen eliminated. The carbon eliminated was also measured, and it was found that 58.4 grams of carbon had been retained in the body. This would correspond to 130 grams of glycogen, but the total amount of glycogen in the body at the end of the experiment was only 35 grams, hence about three fourths of the carbon retained by the cat from the protein food must have been stored as body fat.

The evidence of formation of milk fat in part from protein, while perhaps not amounting to a mathematical demonstration, is still very strong.

Since there is already abundant experimental evidence of the production of carbohydrate from protein and of the transformation of carbohydrate into fat, it is evident that protein food can indirectly, if not directly, contribute to the formation of fat in the body.

The Fate of the Nitrogen in Protein Metabolism

It has already been shown that the nitrogen of the protein of food enters the circulation chiefly, if not wholly, as amino acids and is taken up as amino acids by the various body tissues. The amino acids thus obtained by the tissues from the food serve as material for the building up of body proteins; but in the breaking down of body proteins there is doubtless a liberation of amino acids of the same kinds. Amino acids from either source are subject to deaminization in the tissues, and in so far as α-amino groups are concerned the process doubtless consists chiefly in the splitting out of the nitrogen as ammonia, most of which is later changed to urea. Nitrogen in other forms than α-amino acids may be expected to undergo a somewhat different metabolism, and it is well known that the urine always contains other nitrogen compounds in addition to ammonium salts and urea.

Much light has been thrown upon the chemistry of protein metabolism by the study of the quantitative relations existing among the different forms of nitrogen in the urine under different conditions. For our present purpose it will be sufficient to consider only the more important of the nitrogen compounds of the urine and the relations which they are believed to bear to the processes of normal metabolism.

Urea. — The proteins, on being metabolized in the body, yield varying amounts of arginine, which may undergo hydrolysis into ornithine and urea. In this way a small part of the nitrogen of protein may reach the urea stage through a series of direct cleavages. It is altogether probable, however, that much the greater part of the urea eliminated arises as follows: The protein in catabolism is split to amino acids, which are deaminized (as in the conversion of alanine to methyl glyoxal above mentioned), the nitrogen of the amino group being split out as ammonia, which with the carbonic acid constantly being produced in metabolism forms ammonium carbonate.* Loss of one molecule of water yields ammonium carbamate, which in turn on loss of one molecule of water yields urea.

$$(NH_4)_2CO_3 \rightarrow NH_4CO_2NH_2 + H_2O$$
$$NH_4CO_2NH_2 \rightarrow CO(NH_2)_2 + H_2O$$

Ammonium chloride or sulphate evidently cannot be changed to urea in this way; and experiments show that if hydrochloric or sulphuric acid is introduced into the blood, it is eliminated by the kidneys largely as ammonium salt, and the quantity of urea is correspondingly decreased. In diseased conditions of the liver the organic salts of ammonia (which normally should be burned to carbonate and then converted as above) may also pass through and be eliminated without being changed to urea. In health and on a full protein diet (say about 100 grams protein per day) from 82 to 88 per cent of the total nitrogen excreted by the kidneys is usually in the form of urea. On a low protein diet this percentage is lower.

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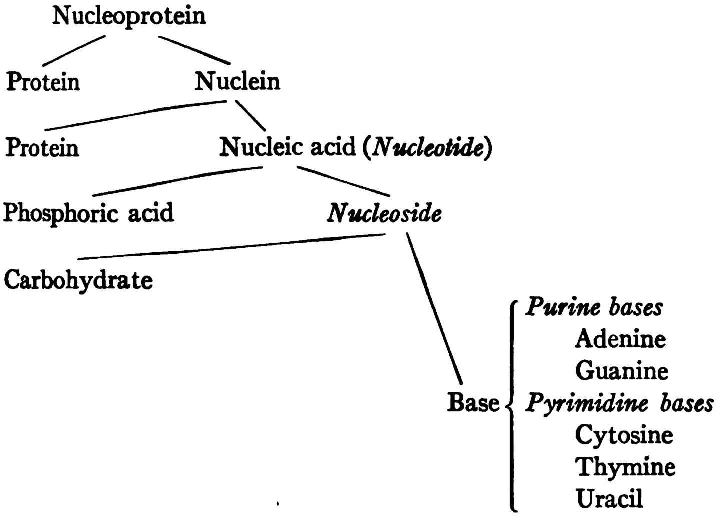
* If ammonium salts of organic acids are first formed, the complete oxidation of the organic acid radicle will bring this ammonia also into the form of carbonate.

Ammonia. — As already noted, ammonia is evidently a normal precursor of urea, being changed to the latter in part in the muscles and other tissues generally and in part during its passage through the liver. In accordance with this view we find that the elimination of nitrogen as ammonia may be notably increased at the expense of urea: (1) in structural diseases of the liver; (2) after injecting mineral acids which combine with ammonia in the body, forming stable ammonium salts; (3) in cases of a pathological excess of acids in metabolism, such as often occurs in diabetes and in fevers. All of these are, of course, abnormal conditions. Normally, about 2 to 6 per cent of the total nitrogen eliminated is in the form of ammonium salts, the amount depending largely upon the relation between the amounts of acid-forming and of base-forming elements in the food, which will be discussed in connection with the study of the ash constituents of food and of mineral metabolism (Chapter X).

Uric acid and the purine bases (nucleic acid metabolism). — A part of the nitrogen of human urine is always in the form of uric acid and purine bases. These owe their origin either to the free purine substances of the food, such as the guanine and hypoxanthine of meat extract, or to the metabolism of nucleic acid derived from the nucleoproteins of the food or of the body tissues. The constituent groups of the nucleic acids and the order of their liberation on hydrolytic cleavage such as occurs in metabolism may be represented by the following diagram adapted from the works of Wells and of Jones:


Nucleoprotein
Protein
Nuclein
Protein
Nucleic acid (*Nucleotide*)
Phosphoric acid
Nucleoside
Carbohydrate
Base
Purine bases
Adenine
Guanine
Pyrimidine bases
Cytosine
Thymine
Uracil

Explanation of diagram. — The distinction between nucleoproteins and nucleins is somewhat arbitrary and perhaps of doubtful value. Wells regards nucleoproteins simply as complexes containing a larger proportion of protein than is contained in nucleins or vice versa. Jones prefers to discuss nuclein metabolism entirely in terms of nucleic acid in order to avoid the danger of unnecessary confusion with protein metabolism. The nucleic acids do not contain any radicles found in simple proteins; they are compounds of phosphoric acid and carbohydrate with purine and pyrimidine bases in which the acid and base radicles are not linked to each other but both to the carbohydrate radicle. Phosphoric acid-carbohydrate-base chains of this sort are called *nucleotides*, and the nucleic acids containing four such chains in the molecule are, in this terminology, *tetranucleotides*. *Nucleotidases* are enzymes which split nucleic acids liberating the phosphoric acid and leaving compounds of carbohydrate with base which are collectively known as *nucleo-*

sides. *Nucleosidases* are enzymes splitting nucleosides into their constituent carbohydrates and bases. In the case of plant nucleic acid the carbohydrate is a pentose (*d*.ribose) and the bases are adenine, guanine, cytosine, and uracil. In animal nucleic acid the carbohydrate is that of a hexose and the bases are adenine, guanine, cytosine, and thymine.

Lusk summarizes the hydrolysis of yeast nucleotides as follows:

Nucleotide—H_3PO_4 →	*Nucleoside*—*d*.ribose →	*Base*
Adenylic acid	→ Adenosine	→ Adenine
Guanylic acid	→ Guanosine	→ Guanine
Cytodin-nucleotide	→ Cytodine	→ Cytosine
Uridin-nucleotide	→ Uridine	→ Uracil

And to show at a glance the characteristic cleavage products of the two types of nucleic acid:

Animal nucleic acid (Thymus)	Plant nucleic acid (Yeast)
Phosphoric acid	Phosphoric acid
Guanine	Guanine
Adenine	Adenine
Cytosine	Cytosine
Thymine	Uracil
Hexose	Pentose

Formulæ and relationships. — The chemical relationships of the purine bases and uric acid so far as these are shown by empirical formulæ are as follows:

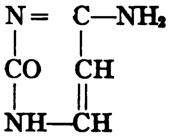
Purine, $C_5H_4N_4$
Adenine, $C_5H_3N_4NH_2$, amino-purine
Guanine, $C_5H_3N_4ONH_2$, amino-oxy-purine
Hypoxanthine, $C_5H_4N_4O$, oxy-purine
Xanthine, $C_5H_4N_4O_2$, dioxy-purine
Uric acid, $C_5H_4N_4O_3$, trioxy-purine

Uric acid, the most highly oxidized of these purines, is the one chiefly found in the urine.

The chemical relations of these substances to each other are more fully shown by the structural formulæ given on this page.

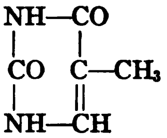
The chemical structure of the pyrimidine bases is indicated by the following formulæ:

Cytosine



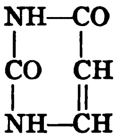
6-amino, 2-oxy-pyrimidine

Thymine



5-methyl, 2, 6-dioxy-pyrimidine

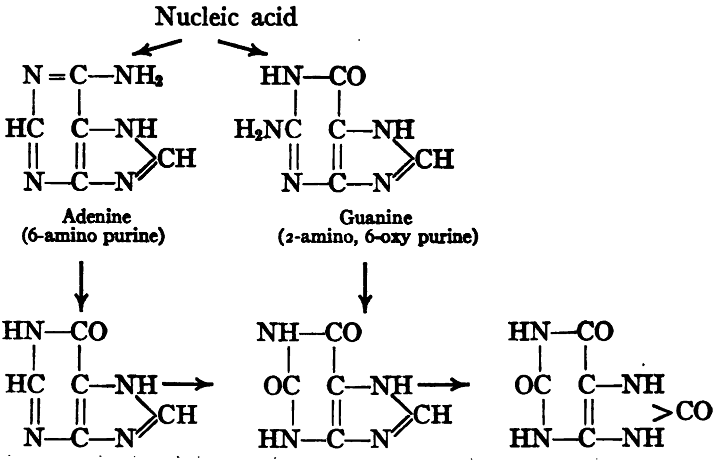
Uracil



2, 6-dioxy-pyrimidine

Since these substances do not yield uric acid or purine bases their fate will not be discussed here.

The mode of origin of uric acid from nucleic acid through the purine bases is as follows:



Nucleic acid

Adenine
(6-amino purine)

Guanine
(2-amino, 6-oxy purine)

Hypoxanthine
(6-oxy purine)

Xanthine
(2, 6-dioxy purine)

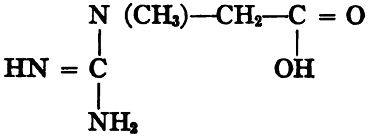
Uric acid
(2, 6, 8-trioxy purine)

Not only is uric acid the most highly oxidized of the purines, but it represents the highest degree to which oxidation can be carried without breaking the purine ring. The extent to which the purine ring is broken and uric acid destroyed in the body varies with the species. In most mammals such "uricolysis" is an important feature of the purine metabolism. In man the power to destroy uric acid seems to have been almost or entirely lost, many recent investigations tending to show that the human body does not contain uricolytic enzymes and that all of the uric acid formed in the body must be transported and excreted either through the kidneys (chiefly in the form of acid urates) or through the intestinal wall.

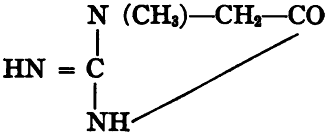
Purines undergoing metabolism in the body may be derived either (1) from the catabolism of nucleoprotein of body tissue or (2) from the food which may contain both nucleoproteins and free purines. Sometimes the term "endogenous uric acid" is applied to that fraction having the former origin, while "exogenous uric acid" indicates that fraction which is directly due to the food. The endogenous uric acid in the urine of man of average size amounts usually to about 0.3 to 0.4 gram per day; the exogenous varies from mere traces to 2 grams or more according to the kind and amount of food consumed. On ordinary mixed diet the total urinary output of uric acid averages about 0.6 to 0.7 gram per man per day. The usual range is about 0.5 to 1.0 gram of uric acid per man per day, in which case the uric acid nitrogen constitutes about 1 to 3 per cent of the total nitrogen of the urine.

Recent investigations of Jones, Levene, and others have greatly elaborated the theory of nucleic acid structure and purine metabolism outlined above. For full discussion the reader is referred to the works of Jones (1914) and Jones and Read (1917).

Creatine and creatinine. — Chemically creatinine is the anhydride of creatine:



Creatine



Creatinine

The biochemical relationships and physiological significance of these substances have been much studied in recent years, and the literature of the subject is far too extensive to be summarized satisfactorily here. The main facts with regard to their elimination as end products of metabolism are: that creatine appears in the urine of children normally and in that of adults during starvation, fevers, and other wasting diseases and when there is impaired functioning of the liver; that normal adults ordinarily excrete little or no creatine but a considerable amount of creatinine. The quantity of creatinine excreted is fairly constant for the individual, averaging about 0.02 gram per kilogram of body weight per day. On ordinary mixed diet the creatinine nitrogen usually constitutes 3 to 7 per cent of the total nitrogen of the urine.

Distribution of excreted nitrogen as influenced by level of protein metabolism. — The above statements regarding the distribution of the eliminated nitrogen among the different end products refer to results obtained upon an ordinary mixed diet containing the usual amount of protein. Folin has shown by a careful and extended study of the urines of healthy men living first upon high and then upon low protein diets, that the distribution of the nitrogen between urea and the other nitrogenous end products depends very largely upon the absolute amount of nitrogen metabolized. In the case of a man who on one day consumed high protein diet free from meat, and a week later was living on a diet of starch and cream, which furnished in all about 6 grams of protein per day, the distribution of end products was changed as shown in the following table:

	On High Protein Diet (Free from Meat)		On Low Protein Diet (Starch and Cream)	
	Grams	Per cent	Grams	Per cent
Total nitrogen	16.8		3.6	
Urea nitrogen	14.7	87.5	2.2	61.7
Ammonia nitrogen	0.49	2.9	0.42	11.3
Uric acid nitrogen	0.18	1.1	0.09	2.5
Creatinine nitrogen	0.58	3.6	0.60	17.2
Undetermined nitrogen	0.85	4.9	0.27	7.3

Thus, on passing from the high protein to the low protein diet (both being free from meat products) there was a marked decrease in both the absolute and the relative amounts of urea, and a decrease in the absolute, but increase in the relative, amount of uric acid, while the absolute amount of creatinine remained unchanged, so that its relative amount was greatly increased.

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CHAPTER VI

THE FUEL VALUE OF FOOD AND THE ENERGY REQUIREMENT OF THE BODY

We have seen that carbohydrate after its absorption into the body may either be oxidized, or stored as glycogen, or transformed into fat; that fat may be oxidized or stored and that at least its glyceryl radicle may be converted into carbohydrate; and that protein absorbed as amino acids may either be built up into body protein, or deaminized and oxidized, or may yield carbohydrate, or may (either directly or indirectly) contribute to the production of fat. It has also been shown that any or all of these foodstuffs may be utilized as fuel for muscular work.

Thus the body is not restricted to the use of any one foodstuff for the support of any one kind of work, but on the contrary has very great power to convert one nutrient into, or use it in place of, another, and so to utilize its resources that the total potential energy of all of these nutrients is economically employed to support the work of all parts of the organism. The carbohydrates, fats, and proteins stand in such close mutual relations in their service to the body that for many purposes we may properly consider the food as a whole with reference to the total nutritive requirements, provided a common measure of values and requirements can be found. Since the most conspicuous nutritive requirement is that of energy for the work of the body, and since these organic nutrients all serve as fuel to yield this energy, the best basis of comparison is that of fuel value, expressed most conveniently in terms of Calories.

Heats of Combustion of the Foodstuffs

The calorific value or heat of combustion of any substance, *i.e.* the amount of energy liberated by the burning of a given quantity of the combustible material, is best determined by means of the bomb calorimeter devised by Berthelot. The particular form of Berthelot bomb which has been most used in the examination of food materials and physiological products is that of Atwater and Blakeslee, fully described by Atwater and Snell in the *Journal of the American Chemical Society* for July, 1903. In outline it consists of a heavy steel bomb with a platinum or gold-plated copper lining and a cover held tightly in place by means of a strong screw collar. A weighed amount of sample is placed in a capsule within the bomb, which is then charged with oxygen to a pressure of at least 20 atmospheres (300 pounds or more to the square inch), closed, and immersed in a weighed amount of water. The water is constantly stirred and its temperature taken at intervals of one minute by means of a differential thermometer capable of being read to one thousandth of a degree. After the rate at which the temperature of the water rises or falls has been determined, the sample is ignited by means of an electric fuse, and, on account of the large amount of oxygen present, undergoes rapid and complete combustion. The heat liberated is communicated to the water in which the bomb is immersed, and the resulting rise in temperature is accurately determined. The thermometer readings are also continued through an "after period," in order that the "radiation correction" may be calculated and the observed rise of temperature corrected accordingly. This corrected rise, multiplied by the total heat capacity of the apparatus and the water in which it is immersed, shows the total heat liberated in the bomb. From this must be deducted the heat arising from accessory combustions (the oxidation of the iron wire used as a fuse, etc.) to obtain the number of Calories * arising from the combustion of the sample.

More recently the adiabatic form of the bomb calorimeter (a modification which avoids the necessity of corrections for heat loss) is coming into more general use. See, for example, the paper by Riche, in the *Journal of the American Chemical Society* for November, 1913.

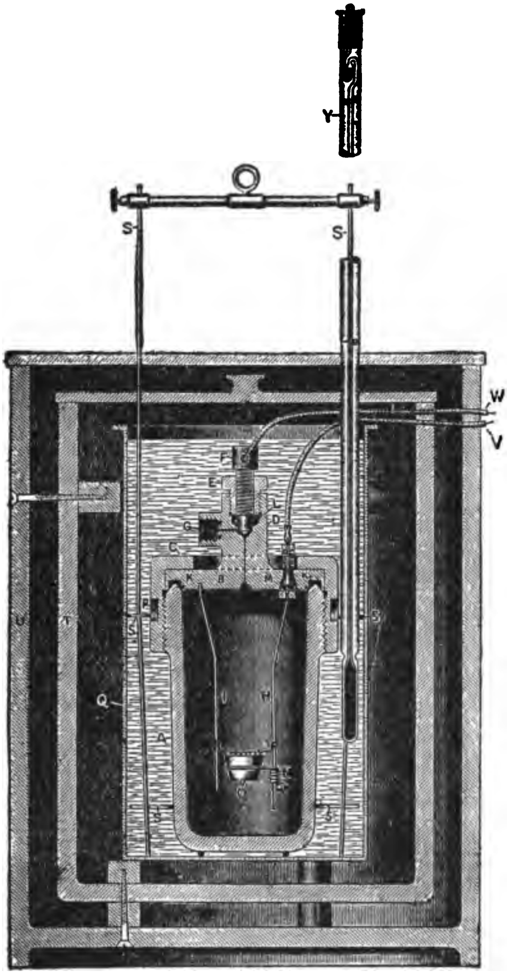

FIG. 6. — The Atwater bomb calorimeter.

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* When the term "Calorie" is used in this work it will be understood to mean the "greater calorie," or "kilogram calorie," *i.e.* the amount of heat required to raise the temperature of one kilogram of water one degree centigrade. This is very nearly the same as the heat required to raise four pounds of water one degree Fahrenheit.

The heat of combustion of organic substances is closely connected with their elementary composition. One gram of carbon burned to carbon dioxide yields 8.08 Calories and 1 gram of hydrogen burned to water yields 34.5 Calories. If a compound consisting of carbon and hydrogen only be burned, it gives nearly the amount of heat which these would give if burned separately.

On the other hand, carbohydrates and fats, being composed of carbon, hydrogen, and oxygen, the carbon and hydrogen are already partly oxidized by the oxygen present in the molecule; so that 100 grams of glucose, for example, containing 40 grams carbon, 6.7 grams hydrogen, and 53.3 grams oxygen, would yield considerably less heat than would be obtained by burning 40 grams of pure carbon and 6.7 grams of pure hydrogen to carbon dioxide and water respectively.

Proteins when burned in the calorimeter give off their carbon as carbon dioxide, their hydrogen as water, and their nitrogen as nitrogen gas.* Thus the nitrogen contributes nothing to and takes nothing from the heat of combustion; and the latter is dependent here, as in the case of carbohydrates and fats, upon the amount of carbon and hydrogen present and the extent to which they are already combined with oxygen. A little additional heat is obtained by the burning of the small amount of sulphur present in the protein.

The relation between the elementary composition and heat of combustion will be made clearer by the following table, which includes a number of typical compounds found in the food or formed in the body.

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* As a matter of fact a small part of the nitrogen is oxidized to nitric acid in the bomb calorimeter, but this is determined and its heat of formation subtracted, so that the final results are as stated above.

Heats of Combustion and Approximate Elementary Composition of Typical Compounds

Substance	Heat of combustion Calories per gram	Carbon per cent	Hydrogen per cent	Oxygen per cent	Nitrogen per cent	Sulphur per cent	Phosphorus per cent
Glucose	3.75	40.0	6.7	53.3			
Sucrose	3.96	42.1	6.4	51.5			
Starch Glycogen	4.22	44.4	6.2	49.4			
Body fat	9.60	76.5	12.0	11.5			
Butter fat	9.30	75.0	11.7	13.3			
Edestin	5.64	51.4	7.0	22.1	18.6	0.9	
Legumin	5.62	51.7	7.0	22.9	18.0	0.4	
Gliadin	5.74	52.7	6.9	21.7	17.7	1.0	
Casein	5.85	53.1	7.0	22.5	15.8	0.8	0.8
Albumin	5.80	52.5	7.0	23.0	16.0	1.5	
Gelatin	5.30	50.0	6.6	24.8	18.0	0.6	
Creatinine	4.58	42.5	6.2	14.1	37.2		
Urea	2.53	20.0	6.7	26.7	46.6		

Since the energy used in the body is obtained from the oxidation of the same kinds of compounds which exist in food, *i.e.* from carbohydrates, fats, and proteins (or their cleavage products), we can estimate the amount of energy transformed in the body if we know the amount of each kind of foodstuff oxidized. Account must, however, be taken of the completeness of the oxidation in each case.

When undergoing complete oxidation in the bomb calorimeter the foodstuffs yield the following average heats of combustion:

Carbohydrates	4.1 Calories per gram.
Fats	9.45 Calories per gram.
Proteins	5.65 Calories per gram.

In the body carbohydrates and fats are oxidized to the same products as in the calorimeter and so yield the same amounts of heat. Protein, however, which burns in the bomb to carbon dioxide, water, and nitrogen, yields in the body no free nitrogen, but urea and other organic nitrogen compounds which are eliminated as end products. These organic nitrogenous end products are combustible; they represent a less complete oxidation of protein in the body than takes place in the bomb. The loss of potential energy calculated on the assumption that all nitrogen left the body as urea would be about 0.9 Calorie per gram of protein, but on account of the elimination of other substances of higher heat of combustion (creatinine, uric acid, etc.), the actual loss in the form of combustible end products is considerably greater and averages about 1.3 Calories for each gram of protein broken down in the body.

Hence, when the body burns material which it has previously absorbed, it obtains:

From carbohydrates	4.1 Calories per gram.
From fats	9.45 Calories per gram.
From protein (5.65 − 1.30 =)	4.35 Calories per gram.

In calculating the fuel value of the food, however, allowance must be made for the fact that a part of each of the materials is lost in digestion.*

The approximate averages on a mixed diet are:

Carbohydrates	2% lost, 98% absorbed.
Fats	5% lost, 95% absorbed.
Protein	8% lost, 92% absorbed.

The approximate *physiological fuel values* of the food constituents are then:

Carbohydrates	4.1 × 98% = 4. Calories per gram.
Fats	9.45 × 95% = 9. Calories per gram.
Protein	4.35 × 92% = 4. Calories per gram.

The figures given by Rubner as representing the fuel values of food constituents are as follows:

Carbohydrates	4.1
Fats	9.3
Protein	4.1

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* The expression "lost in digestion" is here used in the sense explained in Chapter IV.

These were derived from experiments with dogs fed on meat, starch, sugar, etc., and therefore do not allow for so much loss in digestion as has been found to occur with men living on ordinary mixed diet.

Fuel Value of Food Materials

If the composition of a food is known, its approximate fuel value is easily computed by means of the above factors. Thus milk of about average composition contains:

Protein, 3.3 per cent; fat, 4.0 per cent; carbohydrate, 5.0 per cent.

One hundred grams of such milk will furnish in the form of protein ($3.3 \times 4. =$) 13.2 Calories; of fat ($4.0 \times 9. =$) 36.0 Calories; of carbohydrate ($5.0 \times 4. =$) 20.0 Calories; total for 100 grams of milk, 69.2 Calories.

Eggs contain [*] on the average, in the edible portion, 13.4 per cent protein, 10.5 per cent fat, and no appreciable amount of carbohydrate. They would then furnish per 100 grams $(13.4 \times 4) + (10.5 \times 9) = 148.1$ Calories.

Milk and eggs are sufficiently similar to be used interchangeably in the adult dietary within reasonable limits, but evidently they furnish, weight for weight, very different amounts of nutrients and energy. Ordinarily the quantities to be taken as equivalent or mutually replaceable are those which furnish equal fuel value, *e.g.* 100-Calorie portions, the weights of which may be calculated directly from the fuel values of 100 grams.

Thus, for milk — 100 grams furnish 69.2 Calories; then, if x be the number of grams which furnish 100 Calories:

$$100 : 69.2 :: x : 100; \quad x = 145.\dagger$$

Similarly for eggs:

$$100 : 148 :: x : 100; \quad x = 68.$$

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[*] These and all similar statements of average composition are based on Bull. 28, Office of Experiment Stations, U. S. Dept. Agriculture.

[†] It is considered sufficiently accurate to state these quantities to the nearest whole number of grams.

And since the two extremes in the proportion are always the same, the weight in grams of the 100-Calorie portion may always be found by dividing 10,000 (the product of the extremes) by the number of Calories per 100 grams.

The fuel value of foods is often stated in Calories per pound. Thus in the same table (Bull. 28) from which the above figures for composition are taken, the fuel value of milk is given as 325 Calories per pound. Since 453.6 grams furnish 325 Calories, —

$$453.6 : 325 :: x : 100; \quad x = 139.6,$$

the number of grams required to furnish 100 Calories. This figure is about 3 per cent less than the one found above because it is based on a fuel value computed by Rubner's factors, which are 2.5 to 3.3 per cent higher than the factors based on more recent work. (See above.)

The following figures for a few common food materials* are based upon the more recent factors, and show the weight of the 100-Calorie portion in grams and ounces, and the distribution of the calories between proteins, fats, and carbohydrates:

TABLE OF 100-CALORIE PORTIONS † OF FOOD MATERIAL BASED ON THE FACTORS — PROTEIN, 4; FAT, 9; CARBOHYDRATE, 4

FOOD MATERIAL (EDIBLE PORTION)	WEIGHT OF PORTION		DISTRIBUTION OF CALORIES		
	Grams	Ounces	In protein	In fat	In carbohydrates
Beef, free from visible fat	86	3.0	80.4	19.6	
Beef, round steak	64	2.3	54.5	45.5	
Beef, corned	33	1.3	20.9	79.1	
Ham, lean	37	1.2	29.7	70.3	
Ham, fat	19	0.7	11.1	88.9	

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* Arranged according to the classification used in the bulletins of the U. S. Department of Agriculture and in König's well-known reference work *Die Chemie der Menschlichen Nahrungs- und Genussmittel*, viz. meats, fish, eggs, dairy products, grain products, sugars and starches, vegetables, fruits, nuts, oils.

† Table 1 of Appendix B shows 100-Calorie portions of a much larger number of food materials.

Table of 100-Calorie Portions† of Food Material Based on the Factors — Protein, 4; Fat, 9; Carbohydrate, 4 (*Continued*)

Food Material (Edible Portion)	Weight of Portion		Distribution of Calories		
	Grams	Ounces	In protein	In fat	In carbo-hydrates
Bacon, smoked	16	0.6	6.7	93.3	
Codfish	143	5.0	95.0	5.0	
Salmon	49	1.7	43.3	56.7	
Eggs	67	2.3	36.1	63.9	
Milk	145	5.1	19.0	52.0	29.0
Butter	14	0.5	0.5	99.5	
Corn meal	27	1.0	9.0	11.4	79.6
Oatmeal	25	0.9	16.1	16.2	67.7
Rice	28	1.0	9.1	0.7	90.2
Wheat, "entire"	28	1.0	14.7	3.5	81.8
Wheat flour	28	1.0	11.8	2.8	85.4
Bread, white	38	1.3	14.1	4.5	81.4
Sugar	25	0.9			100.0
Asparagus	450	16.0	32.4	8.2	59.4
Beans, dried	29	1.0	26.1	4.7	69.2
Beans, string	240	8.4	22.2	6.5	71.3
Beets	216	7.4	13.8	2.0	84.2
Cabbage	317	11.1	20.3	8.6	71.1
Carrots	220	7.7	9.7	7.9	82.4
Celery	540	19.1	23.8	4.8	71.4
Corn, green or canned	99	3.2	12.2	9.8	78.0
Lettuce	523	18.4	25.2	14.1	60.7
Potatoes	120	4.2	10.5	1.2	88.3
Spinach	418	14.7	35.1	11.3	53.6
Tomatoes	438	15.5	15.7	15.7	68.6
Turnips	253	8.9	13.2	4.6	82.2
Apples	159	5.6	2.5	7.2	90.3
Bananas	101	3.5	5.2	5.4	89.4
Currants, dried	31	1.1	3.0	4.7	92.3
Oranges	194	6.8	6.2	3.5	90.3
Peaches	242	8.5	6.8	2.2	91.0
Pineapple	232	8.2	3.7	6.3	90.0
Plums	118	4.1	4.7		95.3
Prunes, dried	33	1.2	2.8		97.2
Raisins	29	1.0	3.0	8.6	88.4
Almonds	15	0.5	13.0	76.4	10.6
Chestnuts	43	1.5	10.7	16.6	72.7
Peanuts	18	0.6	18.8	63.4	17.8
Olive Oil	11	0.4		100.0	

Since proteins and carbohydrates have the same average fuel value and the ash of food does not as a rule constitute a large percentage, the striking differences in the weights of the various foods required to furnish 100 Calories are usually referable to differences in water content or fat content or both. That beans have nearly 20 times the fuel value of celery is essentially due to the difference in moisture, while the difference in fuel value between lean beef and bacon, or between codfish and salmon, is chiefly a matter of fat content. Meat free from fat is about three fourths water and one fourth protein, and so has a fuel value of about one Calorie per gram, while clear fat has a fuel value about nine times as great.

Fuel values of meats as given in the standard tables are apt to be somewhat misleading, inasmuch as they allow for all the fat ordinarily found on the various cuts as taken from the animal, whereas in many cases a considerable part of this fat is trimmed off by the butcher and treated as a by-product; and often much of the remaining fat is removed either in the kitchen or at the table. If a pound of steak consists of 14 ounces of clear lean, and 2 ounces of clear fat, and the fat is not eaten, at least half of the total fuel value of the pound of steak is lost.

Many vegetables are more watery than lean meats and so contrast even more strikingly with the fats. An ounce of clear fat pork is equal in fuel value to about two pounds of cabbage; an ounce of olive oil to over three pounds of lettuce.

In connection with such comparisons of fuel value, however, it should be emphasized that the fuel value of a food, while of primary importance, is not alone a complete measure of its nutritive value, which will depend in part also upon the amounts and forms of nitrogen, phosphorus, iron, and various other essential elements furnished by the food.

In order to indicate relative richness in nitrogenous constituents (protein), it is not uncommon to state the "nutritive ratio" along with the fuel value of a food. The "nutritive ratio" or "nutrient ratio" is the ratio of non-nitrogenous to nitrogenous nutrients, compared on the basis of fuel values. Since the fuel values of carbohydrates and protein are taken as equal (4 Calories per gram), and that of fats as 2¼ times as great (9 Calories per gram), the nutritive or nutrient ratio may be shown as follows:

$$\text{Carbohydrate} + 2\tfrac{1}{4}\ \text{Fat} : \text{Protein} :: x : 1;$$

or the ratio may be expressed in the form of a fraction:

$$\frac{\text{Carbohydrate} + 2\tfrac{1}{4}\ \text{Fat}}{\text{Protein}}$$

These expressions can, of course, be applied equally well to percentages or to weights of nutrients.

The same information as is given by the statement of fuel value per pound and nutritive ratio may be obtained by comparing the weight of 100-Calorie portions and the percentages of calories supplied by protein as shown in the above table. The statement that 19 per cent of the calories of milk are furnished by protein is equivalent to giving the nutritive ratio of milk as 4.3.

ENERGY REQUIREMENT IN METABOLISM—METHODS OF STUDY AND AMOUNTS REQUIRED FOR MAINTENANCE AT REST

We know definitely from accurate experiments that the "physiological fuel values" which have been deduced represent the energy which is actually obtained by the body from the food and which appears as muscular work or as heat; and we have every reason to suppose that under ordinary conditions the carbohydrates, fats, and proteins each supply the body with the kinds of energy needed for its maintenance and for its work, approximately in proportion to their fuel values as calculated above. We do not now believe that any one nutrient is used to the exclusion of others as a source of energy for any particular function, nor indeed that the body makes any particular distinction between the foodstuffs as sources of energy. The fuel value of the diet as a whole is utilized to meet the energy requirements of the whole body. For the present, therefore, it is the fuel value of the day's dietary which we have to consider rather than the distribution of this as regards protein, fats, and carbohydrates.

The total food (or energy) requirement is best expressed in Calories per day, either for the whole body or per kilogram of body weight, and for convenience of discussion it is usually assumed that the average body weight (without clothing) is for men 70 kilograms (154 pounds) and for women eight tenths as much, 56 kilograms (123 pounds).

There are four important methods of studying the food requirements of man:*

1. By observing the amount of food consumed (dietary studies).

2. By observing the amount of oxygen consumed — preferably also the respiratory quotient (respiration experiments).

3. By determining the balance of intake and output (carbon and nitrogen metabolism experiments).

4. By direct measurement of heat given off by the body (calorimeter experiments).

Dietary studies. — Most dietary studies give little more than a general indication of the food habits of the people studied; but in cases where persons have maintained for a long time the same dietary habits and other conditions of life, and the body weight has remained practically constant, it may be fairly safe to assume that the food has furnished just about the right amount of energy for the maintenance of the body under the observed conditions.

Great care must be taken in drawing inferences from the body weight because of the readiness with which the body gains or loses moisture. Athletes often lose 2 or 3 pounds in an hour of vigorous exercise and regain it in less than a day. Gain or loss of body weight during short periods, therefore, does not by any means necessarily imply a corresponding gain or loss of fat. The body may lose fat and at the same time maintain its weight through gaining water, or vice versa. When, however, the weight remains nearly the same for months at a time, it may usually be assumed that there is no important gain or loss of tissue and that the body is receiving just about the proper amount of total food for its needs. Under these conditions an accurate observation of the food consumed may give valuable indications as to the actual food requirement. Of such dietary studies perhaps the most useful individual example is that of Neumann, who reduced his diet to what appeared to be just about sufficient for his needs and then recorded all food and drink taken during a period of 10 months in which the body weight remained nearly constant. The average daily food furnished:[*]

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* For an account of the historical development of the principles which underlie the measurement of metabolism, see the introductory chapter of Lusk's *Elements of the Science of Nutrition.*

NUTRIENTS	FACTORS	CALORIES	TOTAL CALORIES PER DAY
Protein	66.1 grams × 4. =	264.4	2242
Fat	83.5 grams × 9. =	751.5	
Carbohydrate[†]	306.5 grams × 4. =	1226.0	

The 2242 Calories per day were evidently fully sufficient to meet the energy requirements of this man, whose weight was 66.5 to 67 kilograms (about 147 pounds) and who was engaged at his usual (mainly sedentary) professional work in the Hygienic Institute at Kiel.

Later, when his weight had increased to 71.5 kilograms (157 pounds) as the result of following for a time a more liberal diet (furnishing about 2600 Calories per day), he again observed his dietary while taking what was supposed to be an amount of food sufficient for the maintenance of the body and no more. This second dietary study was continued for 8 months, during which the average daily food consumption was found to be:

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[*] The data are taken from Chittenden's *Nutrition of Man*, page 286.

[†] Including some alcohol (taken in the form of beer), which is estimated as equivalent in fuel value to 1.75 times its weight of carbohydrates.

Nutrients	Factors	Calories	Total Calories per Day
Protein	76.2 grams × 4.	= 304.8	2000
Fat	109.0 grams × 9.	= 981.0	
Carbohydrates *	178.6 grams × 4.	= 714.4	

The body weight remained nearly constant.

These results indicate that this subject, a man of average size, living a normal professional life involving no manual labor in the ordinary sense, but not excluding such muscular movements as are naturally incidental to a sedentary occupation, found his energy requirements satisfied with food furnishing 2000 to 2250 Calories per day.

Respiration experiments. — Since the foodstuffs yield their energy through being oxidized in the body, it is evident that a measure of the energy metabolism can be obtained by finding either the amount of foodstuffs oxidized or the amount of oxygen which is consumed in the process. The apparatus devised and used by Zuntz for this purpose provides a mask, fitting airtight over the mouth and nose and connected by means of valved pipes with apparatus for measuring and analyzing the inspired and expired air. In this way one can determine the volume of oxygen entering, and the volume leaving, the lungs. The difference is the volume consumed in the body.

Benedict has devised an improved form of respiration apparatus in which the subject breathes, either through a mouth- or nose-piece, from a current of air which is purified and kept in circulation in the same manner as that of the respiration calorimeter chamber described below. The carbon dioxide which the man produces is absorbed quantitatively and the oxygen which he consumes is exactly replaced by admitting measured volumes of analyzed oxygen gas from a cylinder of compressed oxygen.

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* Including some alcohol (taken in the form of beer), which is estimated as equivalent in fuel value to 1.75 times its weight of carbohydrates.

A given volume of oxygen used in the body may liberate somewhat different amounts of heat, according as it oxidizes fat, carbohydrate, or protein. For accurate estimations of the energy liberated it is therefore necessary to know the kind of material oxidized, as well as the amount of oxygen consumed. This is calculated from the respiratory quotient.

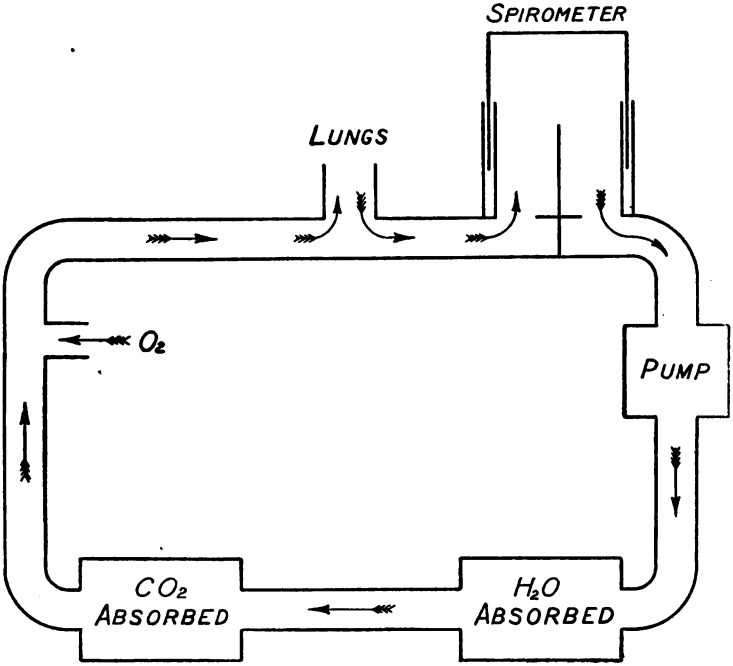

FIG. 7. — Diagram of Benedict respiration apparatus. Courtesy of Dr. F. G. Benedict.

Since the amount of protein broken down in the body can be estimated from the nitrogen excretion, the determination of the respiratory quotient along with the oxygen consumption shows the extent of the combustion in the body and the proportions of fat and carbohydrate burned.* From these data the energy can be calculated.

As a matter of fact it is not necessary to go through the actual calculation of the amounts of fat and carbohydrate burned since the energy derived from a liter of oxygen when used to burn carbohydrate and fat in different proportions can be calculated once for all and expressed in relation to the respiratory quotient as shown in the accompanying table.

ENERGY VALUES OF OXYGEN AND CARBON DIOXIDE AT DIFFERENT RESPIRATORY QUOTIENTS (ZUNTZ AND SCHUMBERG)

RESPIRATORY QUOTIENT	CALORIES PER LITER OF OXYGEN	CALORIES PER LITER OF CARBON DIOXIDE	CALORIES PER GRAM OF CARBON DIOXIDE
0.70	4.686	6.694	3.408
0.71	4.690	6.606	3.363
0.72	4.702	6.531	3.325
0.73	4.714	6.458	3.288
0.74	4.727	6.388	3.252
0.75	4.739	6.319	3.217
0.76	4.752	6.253	3.183
0.77	4.764	6.187	3.150
0.78	4.776	6.123	3.117
0.79	4.789	6.062	3.086
0.80	4.801	6.001	3.055
0.81	4.813	5.942	3.025
0.82	4.825	5.884	2.996
0.83	4.838	5.829	2.967
0.84	4.850	5.774	2.939
0.85	4.863	5.721	2.912
0.86	4.875	5.669	2.886
0.87	4.887	5.617	2.860
0.88	4.900	5.568	2.835
0.89	4.912	5.519	2.810

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* Or, with very little error, it may be assumed that 15 per cent of the oxygen goes to burn protein and the rest is divided between fat and carbohydrate. The values given in the table herewith agree with this assumption. Attention should be called to the fact that estimates of energy metabolism based on carbon dioxide production alone involve larger errors than those based on oxygen consumption alone.

ENERGY VALUES OF OXYGEN AND CARBON DIOXIDE AT DIFFERENT RESPIRATORY QUOTIENTS (ZUNTZ AND SCHUMBERG) (*Continued*)

RESPIRATORY QUOTIENT	CALORIES PER LITER OF OXYGEN	CALORIES PER LITER OF CARBON DIOXIDE	CALORIES PER GRAM OF CARBON DIOXIDE
0.90	4.924	5.471	2.785
0.91	4.936	5.424	2.761
0.92	4.948	5.378	2.738
0.93	4.960	5.333	2.715
0.94	4.973	5.290	2.693
0.95	4.985	5.247	2.671
0.96	4.997	5.205	2.650
0.97	5.010	5.165	2.629
0.98	5.022	5.124	2.609
0.99	5.034	5.085	2.589
1.00	5.047	5.047	2.569

It is then only necessary to determine the respiratory quotient and the volume of oxygen used in order to know the number of Calories of energy metabolized. This is sometimes called the *method of indirect calorimetry.*

This method of studying the total metabolism permits of experiments being carried out very quickly, and is therefore especially useful for the direct investigation of conditions which affect metabolism promptly, such as muscular work or the eating of food. The periods of observation cannot be very long, but the probable results for the 24 hours' metabolism can be estimated by the data obtained during frequent short periods at different times of the day and night. For a critical comparison of this method with the Pettenkofer and Voit method of studying metabolism by the determination of the carbon balance, the reader is referred to the discussion by Magnus-Levy in Von Noorden's *Metabolism and Practical Medicine,* Vol. I, pages 186–198.

From the results of many observations by the Zuntz method Magnus-Levy estimates the minimum metabolism of a man of average size kept absolutely motionless and fasting at 1625

Calories per day. Food barely sufficient for maintenance would increase this by 175, and such incidental muscular movements as would ordinarily be made by a man at rest in bed would involve another 200, making a total of 2000 Calories as the estimated food requirement of a man at rest with a maintenance diet. Magnus-Levy further estimates that the man, if doing no work (in the ordinary sense), but allowed to move about the room instead of remaining in bed, would require 2230 Calories per day.

Carbon and nitrogen balance experiments. — From a comparison of the constituents of the food consumed ("intake") and of the substances eliminated from the body ("output"), the material actually oxidized and the energy liberated in the oxidation may be determined.

The intake is found by weighing and analyzing all food eaten; the output by collecting and determining the end products eliminated through the lungs, the kidneys, the intestines, and sometimes (in very exact experiments) the skin. The time unit in experiments upon the intake and output is almost always 24 hours, the experimental day beginning preferably just before breakfast. The feces belonging to the experimental days are marked, usually by giving a small amount of lampblack with the food as in ordinary digestion experiments, separated and analyzed. The end products given off by the lungs and kidneys during an experimental day are taken as measuring the material broken down in the body during the same period.

Some time is of course required for the elimination of the nitrogenous end products through the kidneys. This unavoidable "lag" in the elimination of nitrogen may introduce an error in determining the nitrogen balance unless the subject has been kept for a few days in advance upon the same diet which is to be used in the experiment.

Assuming that the total nitrogen and carbon of the absorbed food existed in the form of protein, fat, and carbohydrate, and that the amount of carbohydrates in the body is constant from day to day, it is only necessary to determine the carbon dioxide of the expired air and the carbon and nitrogen of the waste products, in order to calculate the amounts of material oxidized and of energy liberated in the body. Experiments of this sort have played a most important part in the development of our knowledge of nutrition. The calculations are usually based on the following average analyses of protein and body fat:

	Protein	Fat
Carbon	53	76.5
Nitrogen	16	—
Hydrogen	7	12
Oxygen	23	11.5
Sulphur	1	—
	100	100

The following data were obtained with a man on ordinary mixed diet:

Calculation of Energy Metabolism from Carbon and Nitrogen Balance. Man of 64 Kilograms at Rest in Atwater Respiration Apparatus

Intake	Grams per Day				
	Protein	Fat	Carbo-hydrate	Nitrogen	Carbon
Total in food	94.4	82.5	289.8	15.1	239.0
Lost in digestion	5.4	3.7	3.2	0.9	7.4
Absorbed	89.0	78.8	286.6	14.2	231.6
Output					
By lungs					207.3
By kidneys				16.2	12.2
Metabolized				16.2	219.5
Balance				− 2.0	+ 12.1

A loss of 2.0 grams body nitrogen indicates (2.0 × 6.25 =) 12.5 grams body protein burned. Also there were 89.0 grams absorbed from food, and, therefore, in all 101.5 grams total protein burned.

Since the respiratory quotient showed that the body was in carbohydrate equilibrium at the beginning and end of each experimental day, *i.e.* at seven o'clock each morning, it may be concluded that the amount of carbohydrate burned was the same as that absorbed from the food, viz. 286.6 grams per day.

From the carbon balance, therefore, we estimate the amount of fat burned as follows:

12.5 grams body protein yield (12.5 × 53 per cent =)	6.6 grams carbon
and there were in the absorbed food	231.6 grams carbon
∴ total available was	238.2 grams carbon
But total catabolized was only	219.5 grams carbon
∴ the body stored in the form of fat	18.7 grams carbon

Since fat contains 76.5 per cent carbon, 1 gram carbon = 1.307 grams fat. ∴ 18.7 grams carbon = 24.4 grams fat.

The body therefore absorbed	78.8 grams fat
stored	24.4 grams fat
burned	54.4 grams fat

In all the body burned per day

101.5 grams protein, yielding	(101.5 × 4.35 * =)	442 Calories
54.4 grams fat, yielding	(54.4 × 9.45 * =)	515 Calories
286.6 grams carbohydrate, yielding	(286.6 × 4.1 * =)	1175 Calories
		2132 Calories

By means of the carbon and nitrogen balance Sonden and Tigerstedt studied the energy metabolism of eight resting men between nineteen and forty-four years of age, with results which varied for the different subjects from 1853 to 2292 Calories per day. Many other experimenters have used the same method with similar results.

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* Here the factors for fuel value are not reduced to allow for loss in digestion, because this loss has already been deducted in computing the amount of each nutrient actually absorbed and rendered available.

Calorimeter experiments. — The most direct, and in some respects most convincing, way of ascertaining the energy metabolism is by the *method of direct calorimetry*. This consists in measuring the total energy expenditure of the body as heat or as heat and mechanical work by confining the subject in a chamber permitting of actual measurement of the heat produced. It was not until the development of the Atwater-Rosa-Benedict respiration calorimeter that complete and satisfactory data covering periods of one to several days were obtained. This apparatus consisted of an air-tight copper chamber, surrounded by zinc and wooden walls with air-spaces between, and was large enough for a man to live in without discomfort, being about 7 feet long, 4 feet wide, and 6½ feet high. An opening in the front of the apparatus, which was sealed during an experiment, serves as both door and window and admits sufficient light for reading and writing. A smaller opening, having tightly fitting caps on both ends, was used for passing food, drink, excreta, etc., into and out of the chamber. The chamber was furnished with a folding bed, chair, and table, and was ventilated by means of a current of air which passed usually at the rate of about 2½ cubic feet per minute. At first this ventilating air current was maintained and measured by means of a specially constructed meter pump which also automatically took samples of the air for analysis. Later the apparatus was so modified as to make use of the same air throughout an experiment, the carbon dioxide and water given off by the subject being removed by circulating the air through purifying vessels, and the oxygen which the subject uses being replaced by adding weighed amounts of oxygen to the air current as required.* By this means it is possible to carry out, in the

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* **Figure 8 indicates diagrammatically the ventilating system as applied in one of the later forms of apparatus.**

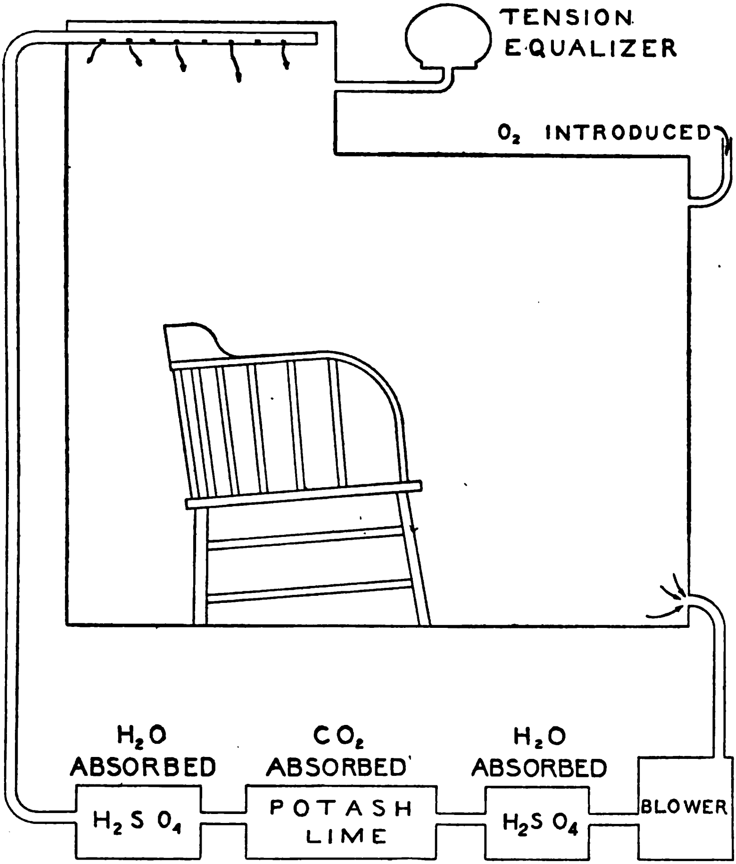
TENSION EQUALIZER
O_2 INTRODUCED
H_2O ABSORBED
CO_2 ABSORBED
H_2O ABSORBED
H_2SO_4
POTASH LIME
H_2SO_4
BLOWER

FIG. 8. — Diagram of ventilation of respiration calorimeter. The air is taken out at lower right-hand corner and forced by the blower through the apparatus for absorbing water and carbon dioxide. It returns to the calorimeter at the top. Oxygen can be introduced into the chamber itself as need is shown by the tension equalizer. Courtesy of Dr. F. G. Benedict and the Carnegie Institution of Washington.

calorimeter, metabolism experiments in which the oxygen and hydrogen as well as the carbon and nitrogen balances are determined, and from these data the gain or loss of carbohydrate as well as of protein and fat can be determined.

The ventilating air current is so regulated that it enters and leaves the calorimeter at the same temperature; and between the copper and zinc walls are placed a large number of thermo-electric junctions connected with a delicate galvanometer by means of which each wall is tested every four minutes, day and night, during the progress of an experiment, and the minute amounts of heat which may pass to or from the calorimeter through its walls are quickly detected and made to balance each other. Thus there is no gain or loss of heat either through the walls of the chamber or by the ventilating air current, and the heat given off by the subject can leave only by the means especially provided for carrying it out and measuring it. A part of the heat liberated is carried from the chamber in latent form by the water vapor in the outgoing air, which is accurately determined. The rest of the heat is brought away by means of a current of cold water circulating through a copper pipe coiled near the ceiling of the chamber. The quantity of water which passes through the pipe and the difference between the temperature at which it enters and that at which it leaves the coil are carefully determined and show how much heat is thus brought out of the chamber.

In recent years several different calorimeters, based on the principles of the apparatus just described but adapted in size and shape to different types of experimentation, have come into use. Notable among these are the "chair" and the "bed" calorimeters, which are so constructed as to accommodate a subject in the sitting or reclining position in comfort but in a minimum of space; for only by making the calorimeter chamber small is it practicable to obtain a high degree of

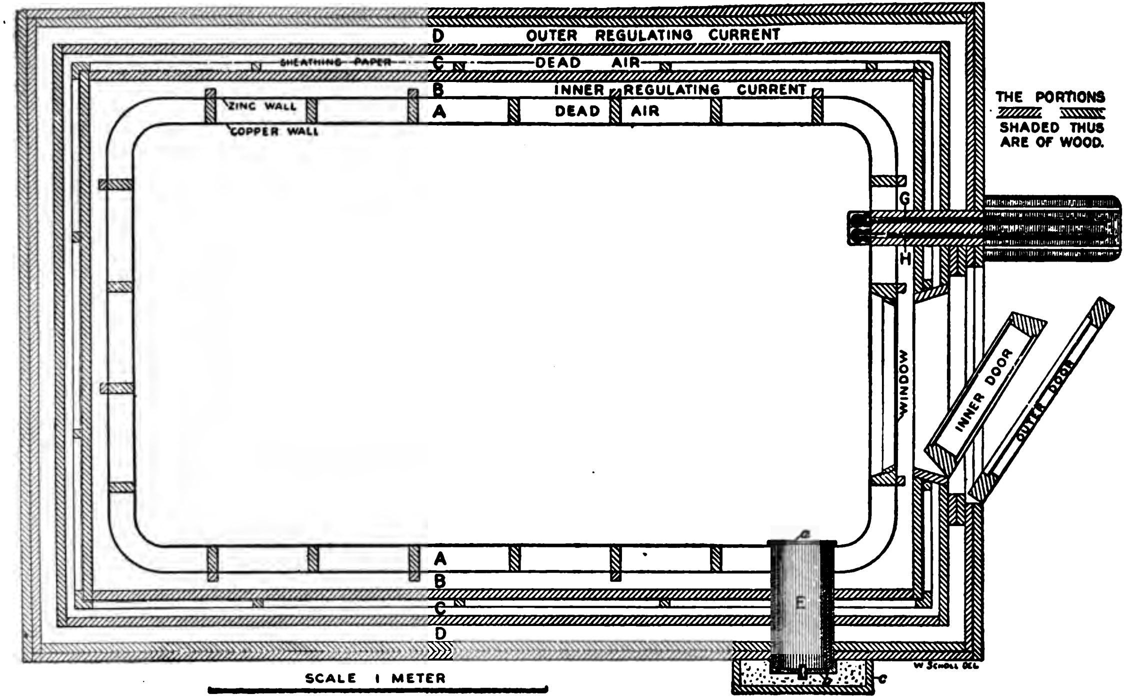
D
OUTER REGULATING CURRENT
C
SHEATHING PAPER
DEAD AIR
B
INNER REGULATING CURRENT
A
DEAD AIR
ZINC WALL
COPPER WALL
THE PORTIONS ▨ ▧ SHADED THUS ARE OF WOOD.
G
H
WINDOW
INNER DOOR
OUTER DOOR
E
A
B
C
D
W SCHOLL DEL
SCALE 1 METER

FIG. 9. — Horizontal section of the original Atwater-Rosa-Benedict respiration calorimeter. Courtesy of the United States Department of Agriculture.

accuracy in experiments of a few hours' duration. Figures 9, 10, and 11 show sectional diagrams of the original calorimeter chamber and of the more recent chair and bed calorimeters respectively.

Detailed and illustrated descriptions of the chief forms of apparatus now in use may be found in the publications by Benedict and Carpenter, by Langworthy and Milner, and by Lusk, Riche, and Soderstrom, full references to which are given at the end of this chapter.

By means of the Atwater-Rosa-Benedict apparatus and its various modifications, it has been possible to measure the heat production or energy expenditure of a man for a day or for a period of days very accurately. In the original Atwater-Benedict series it was found that the difference in results determined by direct and indirect calorimetry was rarely as much as 2 per cent, and in the average of 45 experiments covering a total of 143 days the difference was only 0.01 per cent. The results obtained by direct energy measurements are therefore the same as those computed from respiration and metabolism experiments when the technique is of the best and the experiments are sufficiently prolonged. This agreement is in general less exact in individual experiments in proportion as the experimental periods are shortened; but the methods are now so highly developed that the results of direct and indirect calorimetry are considered practically interchangeable even for experiments of a few hours' duration. In 1913 Armsby compiled the following summary of experiments both upon men, dogs, and cattle which had been published up to that time. It will be seen that the difference between the total heat production as computed and as directly measured is only one fourth of one per cent, or quite within the limits of accuracy of experimental methods of this sort.

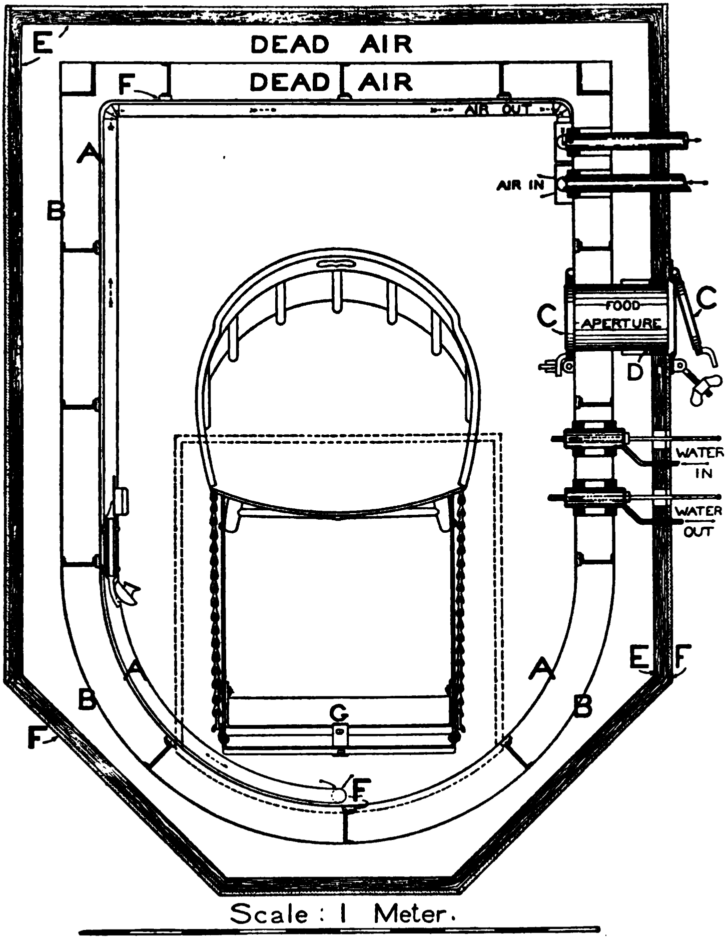
E
DEAD AIR
F
DEAD AIR
AIR OUT
A
B
AIR IN
C
FOOD APERTURE
C
D
WATER IN
WATER OUT
E
F
A
B
A
B
F
G
F
Scale : 1 Meter.

FIG. 10. — Horizontal cross-section of chair calorimeter, showing cross-section of copper wall at *A*, zinc wall at *B*, hair-felt at *E*, and asbestos outer wall at *F*; also cross-section of all upright channels in the steel construction. At the right is the location of the ingoing and outgoing water and the thermometers. At *C* is shown the food aperture, and *D* is a gasket separating the two parts. The ingoing and outcoming air-pipes are shown at the right inside the copper wall. The telephone is shown at the left, and in the center of the drawing is the chair with its foot-rest, *G*. In dotted line is shown the opening where the man enters. Courtesy of Dr. F. G. Benedict and the Carnegie Institution of Washington.

EXPERIMENTER	TOTAL NUMBER OF DAYS	TOTAL COMPUTED HEAT PRODUCTION CALORIES	TOTAL OBSERVED HEAT PRODUCTION CALORIES	PERCENTAGE DIFFERENCE
Rubner	45	17,406	17,350	− 0.32
Laulanié	7	1,865	1,859	− 0.31
Atwater and Benedict .	93	249,063	248,930	− 0.05
Benedict and Milner .	24	95,075	95,689	+ 0.65
Benedict	53	102,078	101,336	− 0.73
Armsby and Fries . .	114	976,204	980,234	+ 0.41
	336	1,441,691	1,445,398	+ 0.26

As Armsby points out: "These results may be taken as demonstrating that the animal heat arises exclusively from the combustions in the body, but they have a much broader significance. They show that the transformations of chemical energy into heat and work in the animal body take place according to the same general laws and with the same equivalencies as in our artificial motors and in lifeless matter generally. The great law of the conservation of energy rules in the animal mechanism, whether in man, carnivora, or herbivora, just as in the engine. The body neither manufactures nor destroys energy. All that it gives out it gets from its food, and all that is supplied in its food is sooner or later recovered in some form."

Since the time of Armsby's compilation the agreement between the observed and computed heat production has been confirmed in many additional experiments, and both by the same and different experimenters.

Working with the original Atwater calorimeter, Atwater and Benedict conducted "rest" experiments upon six different men who lived in the calorimeter as quietly as was feasible for days at a time, taking as a rule but little more exercise than was involved in dressing and undressing, folding and unfolding the bed, table, and chair, taking samples and observations pertaining to the experiment, writing, etc., in short, the life of a healthy man, confined to one small room.

The average daily metabolism of each of the subjects was as follows:

SUBJECT	AGE YEARS	WEIGHT AVERAGE	NUMBER OF EXPERIMENTS	TOTAL EXPERIMENTAL DAYS	CALORIES PER DAY
E. O.	31–34	70 K. (154 lb.)	13	42	2283
A. W. S.	22–25	70 K. (154 lb.)	4	9	2337
J. F. S.	29	65 K. (143 lb.)	4	12	2133
J. C. W.	21	76 K. (168 lb.)	1	4	2397
H. F.	54	70 K. (154 lb.)	1	3	1904
B. F. D.	23	67 K. (147 lb.)	1	3	2228
Mean of individual averages . . .	. . .	. . .	. . .	. . .	2213

Extreme deviations from the mean, + 184 to – 309 Calories,
or + 8.4 to – 14 per cent.

Omitting the results obtained with the one subject who was considerably older than the others, the figures become as follows:

Mean of individual averages, 2277 Calories.
Extreme deviations from mean, + 120 to – 144. Calories,
or + 5.2 to – 6.3 per cent.
Deviations in body weight, + 8.7 to – 7.1 per cent.

The subject "H. F.," aged fifty-four, who believed that he consumed only half the usual amount of food, had a food requirement about 15 per cent less than that of the younger men averaging about the same weight. The five younger men varied in age from twenty-one to thirty-four years, were natives of three different countries, and had been accustomed to very different dietary habits and modes of life, yet they differed less in energy requirements than in body weight.

Summary of the Evidence Obtained by the Different Methods

A general view of the results obtained by all four of the methods described shows them to be strikingly consistent and leads to the conclusion that the food requirements of a young to middle-aged man of average size, without muscular work, eating a mixed diet sufficient to meet his need, approximates 2000 Calories per day, and that such muscular activity as is incidental to very quiet living indoors may be expected to raise this requirement to about 2200 Calories per day.

Lusk summarizes the mean energy requirement of an average sized man in somewhat more precise terms as follows:

Absolute rest in bed without food	1680 Calories
Absolute rest in bed with food	1840 Calories
Rest in bed, 8 hours, sitting in chair 16 hours, with food	2168 Calories

The very close agreement in results reached by many independent investigators, using four distinct methods of study, must be taken as establishing the approximate average food requirement of a man at rest beyond any reasonable doubt.

Significance of Basal Energy Metabolism

On account of the great importance of the fundamental energy expenditure both for the study of normal nutrition, and as a basis for comparison in the investigation of disease, the experiments above described have been followed by others designed to establish with even greater exactness the "basal metabolism" which goes on when the direct effect of food is excluded and when muscular activity is suppressed as completely as possible. Experiments of this latter type must necessarily be carried out in shorter periods than were used in the Atwater investigations described above. Being shorter, they

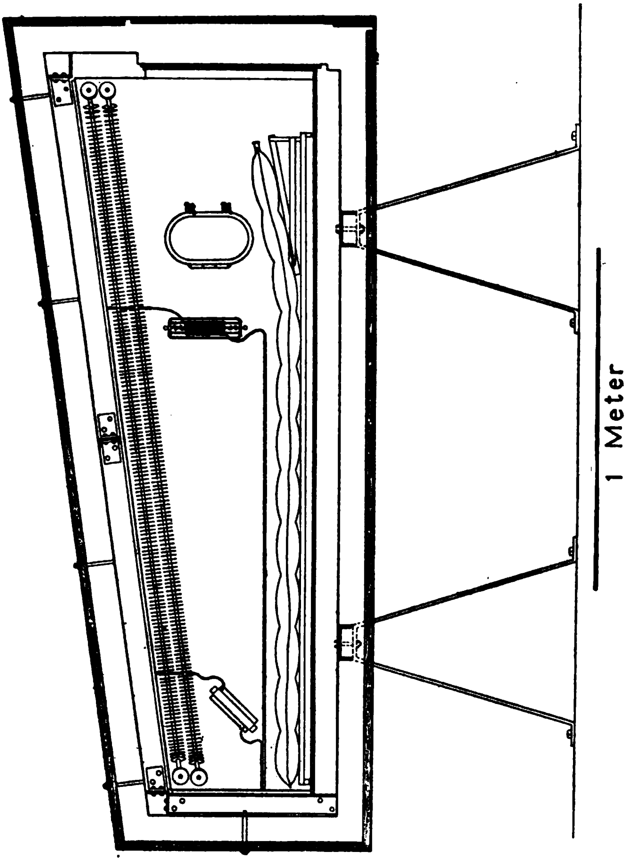

FIG. 11.—Vertical cross-section of bed calorimeter, showing part of steel construction, also copper and zinc walls, food aperture, and wall and air-resistance thermometers, and heat absorbers. Courtesy of Dr. F. G. Benedict and the Carnegie Institution of Washington.

can be more frequently repeated and more readily extended to cover a larger number of individuals.

Data obtained in such studies of "basal metabolism" will be cited later in connection with the study of the various conditions which influence the energy metabolism and total food requirement.

A systematic analysis of the maintenance requirement of the body with reference to its principal functions has not yet been made, but results obtained by Armsby, Atwater, Benedict, Lusk, Magnus-Levy, Rubner, Zuntz, and others indicate that in the healthy adult the expenditure of energy when at rest and no longer influenced by the direct effect of food ("basal energy metabolism") may be attributed in part, perhaps up to one tenth, to the work of the heart in maintaining the circulation; from one tenth to two tenths to the muscular work of respiration; from one third to one half, or perhaps even more, to the maintenance of muscular tonus (tone, tension, elasticity); and an unknown fraction to other forms of internal work.

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CHAPTER VII

CONDITIONS GOVERNING ENERGY METABOLISM AND TOTAL FOOD REQUIREMENT

ACTIVITY, age, and size are the most important factors affecting the total food requirement of the body, but several other conditions, such as bodily constitution and environment, may have measurable influence. Since the food requirement of the adult is more accurately known than that of the growing organism, it will be best to consider the conditions affecting the energy metabolism of the adult first and the demands of growth later.

Basal Metabolism of the Adult

The basal rate of energy metabolism, as shown by the heat production (determined either by direct or indirect calorimetry) at complete rest and at a sufficiently long time after the last meal to eliminate the direct effects of food, has now been studied in considerable detail. In the healthy adult this basal metabolism depends chiefly upon the size, shape, and composition of the body and the activity of certain internal processes. It may or may not be appreciably influenced by the temperature of the surroundings.

Influence of the size, shape, and composition of the body. — For different adults of the same species the energy metabolism and therefore the total food requirement as a rule increases with the size, but not to the same extent that the body weight increases; so that the requirement, though greater in absolute amount, is less per unit of body weight in the larger individual than in the smaller. The energy metabolism increases in proportion to the surface rather than the weight. Thus, Rubner collected the following data from experiments upon seven different dogs, all full grown but differing greatly in size.

No.	Body Weight Kilograms	Heat Production in Calories per Day		
		Total	Per kilogram of body weight	Per square meter of body surface
I	3.10	273.6	88.25	1214
II	6.44	417.3	64.79	1120
III	9.51	619.7	65.16	1183
IV	17.70	817.7	46.20	1097
V	19.20	880.7	45.87	1207
VI	23.71	970.0	40.91	1112
VII	30.66	1124.0	36.66	1046

Here the heat production in calories per kilogram was over twice as great in the smallest as in the largest dog, but the total metabolism was nearly proportional to the surface area throughout.

That the relationship of energy metabolism to body surface is not due simply to loss of heat through the cooling effect of the environment will be apparent from the observations upon the regulation of body temperature.

Armsby, in his *Principles of Animal Nutrition,* quotes the explanation offered by von Hösslin — that the internal work and the consequent heat production in the body are substantially proportional to the two thirds power of its volume, and since the external surface bears the same ratio to the volume, a proportionality necessarily exists between heat production and surface.

Largely as the result of Rubner's work, it became customary to express energy requirements in terms of surface; but, on account of the difficulties involved in actual measurements, the surface was customarily computed from the weight, usually by Meeh's formula $S = W^{\frac{2}{3}} \times C$ or $S = 12.3\sqrt[3]{W^2}$, in which S represents the surface and W the weight, the constant 12.3 having been found by Meeh in a series of measurements of men.

Benedict found that the basal metabolism of normal men and women per unit of surface as computed from the weight by the Meeh formula is by no means constant, varying from 29 to 40 Calories per square meter per hour among 89 men, and from 26 to 38 Calories per square meter per hour among 68 women.

Recently DuBois and DuBois have made a new series of measurements of body surface in which they find that Meeh's formula gives results which are much too high, probably because Meeh's measurements were made on thin men. Tabulating the results of other measurements with their own, they find that among the 20 cases of direct measurements of body surface which had been reported up to 1915, the errors in results computed by Meeh's formula range from −7 to +36 per cent. Differently stated, if the principle of Meeh's formula be employed it would be necessary to vary the " constant " from 9.06 to 13.17 in order to express the relationships of weight and surface actually found among these 20 individuals.

The errors involved in computing the surface from the weight alone are therefore much greater than were formerly supposed. DuBois and DuBois have devised two new methods by which the surface may be computed with much greater accuracy: (1) from a series of nineteen measurements of different parts of the body, the surface of each part being computed and the results added together (" linear formula "), and (2) a " height-weight formula " which these authors have derived mathematically from the data of all available measurements of height, weight, and surface.

The height-weight formula may be written thus:

$$A = W^{0.425} \times H^{0.725} \times C$$

or in the form:

$$\text{Log } A = (\text{Log } W \times 0.425) + (\text{Log } H \times 0.725) + 1.8564$$

in either of which

A = Surface area in square centimeters
H = Height in centimeters
W = Weight in kilograms
C = A constant (71.84)

In connection with this formula the authors give also a chart * from which the approximate surface area may be obtained at a glance if height and weight are known. The data given in the accompanying table have been taken from the DuBois chart.

TABLE SHOWING **Surface Area in Square Meters** FOR DIFFERENT HEIGHTS AND WEIGHTS ACCORDING TO THE HEIGHT-WEIGHT FORMULA OF DUBOIS AND DUBOIS

HEIGHT IN CENTIMETERS	WEIGHT IN KILOGRAMS																
	25	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100	105
200							1.84	1.91	1.97	2.03	2.09	2.15	2.21	2.26	2.31	2.36	2.41
195						1.73	1.80	1.87	1.93	1.99	2.05	2.11	2.17	2.22	2.27	2.32	2.37
190				1.56	1.63	1.70	1.77	1.84	1.90	1.96	2.02	2.08	2.13	2.18	2.23	2.28	2.33
185				1.53	1.60	1.67	1.74	1.80	1.86	1.92	1.98	2.04	2.09	2.14	2.19	2.24	2.29
180				1.49	1.57	1.64	1.71	1.77	1.83	1.89	1.95	2.00	2.05	2.10	2.15	2.20	2.25
175	1.19	1.28	1.36	1.46	1.53	1.60	1.67	1.73	1.79	1.85	1.91	1.96	2.01	2.06	2.11	2.16	2.21
170	1.17	1.26	1.34	1.43	1.50	1.57	1.63	1.69	1.75	1.81	1.86	1.91	1.96	2.01	2.06	2.11	
165	1.14	1.23	1.31	1.40	1.47	1.54	1.60	1.66	1.72	1.78	1.83	1.88	1.93	1.98	2.03	2.07	
160	1.12	1.21	1.29	1.37	1.44	1.50	1.56	1.62	1.68	1.73	1.78	1.83	1.88	1.93	1.98		
155	1.09	1.18	1.26	1.33	1.40	1.46	1.52	1.58	1.64	1.69	1.74	1.79	1.84	1.89			
150	1.06	1.15	1.23	1.30	1.36	1.42	1.48	1.54	1.60	1.65	1.70	1.75	1.80				
145	1.03	1.12	1.20	1.27	1.33	1.39	1.45	1.51	1.56	1.61	1.66	1.71					
140	1.00	1.09	1.17	1.24	1.30	1.36	1.42	1.47	1.52	1.57							
135	0.97	1.06	1.14	1.20	1.26	1.32	1.38	1.43	1.48								
130	0.95	1.04	1.11	1.17	1.23	1.29	1.35	1.40									
125	0.93	1.01	1.08	1.14	1.20	1.26	1.31	1.36									
120	0.91	0.98	1.04	1.10	1.16	1.22	1.27										

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* Reproduction of the chart may be found on page 126 of the third edition of Lusk's *Science of Nutrition*.

On applying the "height-weight formula" to the recorded energy metabolism of the large number of men studied in Benedict's laboratory, as well as in his own, DuBois finds that all the data for men under 50 years of age are within 15 per cent of the average basal heat production of 39.7 Calories per hour per square meter of surface area properly computed, and that 86 per cent of all the cases are within 10 per cent of the average. Means, using the more accurate "linear formula," finds all of his 16 normal cases (9 men and 7 women) and also most of his obesity cases to fall within DuBois' "normal limits" (*i.e.* within 10 per cent of DuBois' average of 39.7 Calories per square meter per hour). DuBois[1] believes that one may "feel certain that with men between the ages of 20 and 50 the (basal) metabolism of each individual is proportional to his surface area whether he be short or tall, fat or thin."

Differences of build (shape of body) are associated not only with varying ratios of weight to surface but also with differences of fatness, *i.e.* of body composition. The thin man, besides having a greater surface in proportion to his weight, differs also from the stout man in that a larger percentage of his body is actual protoplasm. Since the metabolism of the body depends more upon its weight of protoplasm (active tissue) than upon its total weight, we have here an important reason for believing that the food requirement will be greater in a tall, thin man than in a shorter and fatter man of the same weight.

Von Noorden tested this question by observing the metabolism (for one day without food) of two men of different build but nearly the same weight. The results were as follows: 1st man, thin and muscular, weight 71.1 kilograms — 2392 Calories = 33.6 Calories per kilogram; 2d man, stout, weight 73.6 kilograms — 2136 Calories = 29.0 Calories per kilogram. These two men had nearly the same weight but differed in height, in body composition, and in energy expenditure.

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[1] *American Journal of the Medical Sciences*, June, 1916, page 786.

Even with the same height and weight there may be differences in the composition of the body. Thus a man of average height and weight but large-boned and loosely built will be of less than average fatness; a man of the same height but less broad-shouldered must be somewhat fatter in order to weigh the same. Hence equality of height and weight does not necessarily imply the same shape and composition of body. Benedict finds among normal adults of like height and weight the basal metabolism of athletes about five per cent higher, and that of women about five per cent lower, than that of average non-athletic men. He attributes these divergencies to differences in body composition, holding that women have somewhat more fat, and athletes somewhat less, than non-athletic men of the same weight and height.

Internal activities. — The work of maintaining the ***respiration and circulation*** evidently involves a continual expenditure of energy. It is clear too that deep and rapid breathing or vigorous heart action must involve an increased activity of the muscles concerned. But it is not always clear to what extent increased respiratory and heart action are a cause and to what extent they are an effect of increased energy metabolism. Thus Murlin and Greer[1] emphasize the close relationship of the heart to the requirements of the tissues for energy in that the energy metabolism is immediately dependent upon oxygen supply. Since but little available oxygen can be stored in the living substance, "the response of the heart to variations in the (energy) requirement must be immediate and, within very narrow limits of time, proportional to this requirement." And Benedict states that:

If subject A, in a resting post-absorptive condition, has on a given day a pulse rate of 70 per minute, and on a subsequent day under exactly the same conditions has a pulse rate of 60 per minute, it may be asserted with every degree of confidence that the metabolism on the second day will be perceptibly, indeed measurably, lower than the first.

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[1] *American Journal of Physiology*, Vol. 33, page 253.

A large factor in basal metabolism is the maintenance of *muscular tension* or *tone*. That every living muscle is always in a state of tension is evident from the fact that it gapes open if cut. It is equally evident that the degree of tension (and therefore the expenditure of energy required to maintain it) varies greatly in different individuals under similar conditions and in the same individual under different conditions. The differences observed by Atwater and Benedict between the metabolism of the sleeping hours and that of the hours spent sitting up without muscular movement (65 and 100 Calories respectively) are largely due to the more complete relaxation of the muscles during sleep. Thus there is in the "resting" muscle a continual expenditure of energy which first takes the form of muscular tension, or tone, but ultimately appears as heat, so that the heat production, or energy metabolism, of the body at rest depends to a considerable extent upon the degree of tension which still persists in the muscles.

Benedict and Carpenter report the following figures in Calories per hour, for the energy metabolism during sleep (1 A.M. to 7 A.M.) following different conditions of activity and showing the after effects of work upon muscular tension during rest:

ENERGY METABOLISM DURING SLEEP — CALORIES PER HOUR

SUBJECT	SLEEP AFTER REST	SLEEP AFTER MODERATE WORK	SLEEP AFTER SEVERE WORK	SLEEP AFTER VERY SEVERE WORK
E. O.	69.3	74.8	—	—
J. F. S.	60.4	65.3	—	—
J. C. W.	77.2	—	83.1	—
B. F. D.	69.8	—	83.3	—
A. L. L.	78.3	—	83.7	97.9

Benedict also finds that even under the most quiet conditions a higher tension gradually develops during the waking hours. A fasting man metabolized when lying at complete rest 14 per cent more in the morning than when sound asleep at night, and 22 per cent more in the late afternoon than when asleep.

Does mental work influence energy metabolism? — In any consideration of this question it is important to distinguish sharply between the nervous control of muscular conditions and the metabolism of the brain and nerve substance itself. As emphasized particularly by Mathews, the brain receives a copious blood supply, and the blood coming to the brain is arterial, while that leaving the brain is venous, indicating that considerable oxidative metabolism occurs in brain tissue. Recently also Tashiro has shown that the carbon dioxide production of nerve fiber is increased when the nerve is stimulated to activity. But since the entire weight of brain and nerve substance constitutes only about 2 per cent of the body weight, it remains questionable whether, even if its metabolism increases with "mental activity," the increase would be appreciable in measurements of the energy expenditure of the body as a whole. Probably the best-controlled experiments upon this problem, certainly the ones affording most accurate measurement of the energy expenditure, are those of Benedict and Carpenter, in which a number of college students were given course examinations in the respiration calorimeter and their energy metabolism during the three-hour period covered by the examination was compared with that during the same period on another day when the student sat in the calorimeter at rest. In some individuals the metabolism was higher during the examination period, while in others it was lower — results much more likely due to involuntary increase or decrease of muscular tension than to altered metabolism of the brain tissue. In the average of the entire series of experiments there appeared a slight increase of oxygen consumption, carbon dioxide output, and heat production during the examination, but the increase was so small and the exceptions so numerous that the investigators were not willing to conclude from their results that mental work has any positive effect upon the total metabolism, but rather infer the opposite.

Apparently we must conclude that such changes in energy metabolism as may result from differences in activity of the brain and nerves involved in the performance of mental work are so small, in comparison with the energy exchanges always going on in the muscles, that the former are quite obscured by the unavoidable fluctuations of the latter, and so play no measurable part in determining the total food requirement of the body.

Internal secretions, notably that of the thyroid gland, may exert a significant influence upon energy metabolism through augmenting the heart action and respiration rate, probably also through heightened muscular tension, and possibly in other ways. Lusk says: "With the possession of such a gland as the thyroid, whose suppression may diminish metabolism twenty per cent and whose stimulation may increase it 100 per cent, it is truly strange that the normal person should have a basal metabolism so regulated as to correspond to a definite heat loss per square meter of body surface." If, however, the thyroid gland is conspicuously over- or under-developed in size or activity the condition is regarded as a departure from health (goiter, myxedema); the effect of these and some other diseases upon energy metabolism has been summarized recently by DuBois[1] as follows:

"Basal metabolism is higher than normal in exophthalmic goiter, in fever, in lymphatic leukemia and pernicious anemia, in severe cardiac disease, and in some cases of severe diabetes and cancer. It is lower than normal in cretinism and myxedema, in old age, in some wasting diseases, and perhaps in some cases of obesity." "Diseases of the ductless glands other than thyroid show in some cases an increase, in some a decrease; but these are comparatively small."

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[1] *Archives of Internal Medicine*, Vol. 17, page 916 (1916).

Benedict[1] also holds, in opposition to some other authorities, that "when a carbohydrate-free diet is eaten an *acidosis* is developed which distinctly increases the cellular activity and results in a very noticeable increase in the basal metabolism."

In a recent general review of the factors affecting normal basal metabolism Benedict[2] concludes "that the basal metabolism of an individual is a function, first, of the total mass of active protoplasmic tissue, and, second, of the stimulus to cellular activity existing at the time the measurement of the metabolism was made." And that: "Perhaps the most striking factors causing variations in the stimulus to cellular activity are age, sleep, prolonged fasting, character of the diet, and the after effect of severe muscular work."

Influence of Muscular Work upon Metabolism and Food Requirement

Muscular work is much the most important of the factors which raise the food requirements of adults above the basal rate necessary for mere maintenance.

Accurate measurements by means of the calorimeter have shown that the average total metabolism of a man sitting still is about 100 Calories per hour; while the same man working actively increases his metabolism up to about 300 Calories per hour; and a well-trained man working at about his maximum capacity metabolizes material enough to liberate 600 Calories per hour, *i.e.* his metabolism may be six times as active during the hours actually spent in such work as when he is at rest. If during 24 hours a man works as hard as this for 8 hours and spends 2 hours in such light exercise as going to and from work, his food requirement for the day will be somewhat over 6000 Calories, or three times the maintenance requirement. Thus, work may increase the day's metabolism as much as 200 per cent, whereas liberal feeding at the end of a fast was found to increase the metabolism only 22.5 per cent, or one ninth as much. Only a few exceptional occupations, such as that of lumbermen, for example, involve such heavy work as to cause a metabolism of 6000 Calories per day. More often the man who works 8 hours a day at manual labor will increase his metabolism by 1000 to 2000 Calories above what is needed for maintenance at rest, making his total food requirement 3000 to 4000 Calories.

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[1] *Journal of Biological Chemistry*, Vol. 18, page 141 (July, 1914).

[2] *Proceedings of the National Academy of Sciences*, Vol. 1, pages 105–109.

Voit estimated the food requirement of a "moderate worker" at about 3050 Calories; and Atwater, in adapting this standard to American conditions, increased the allowance to 3400–3500 Calories in the belief that the American works more rapidly and therefore with a greater expenditure of energy. The mistake is often made of supposing that these estimates were intended for every one who leads an active life, whereas they really contemplate a long day of manual labor, for Voit's definition of "moderate worker" was a man laboring 9 or 10 hours a day at an occupation such as that of a carpenter, mason, or joiner.

The amount of energy spent during 24 hours by a sedentary worker will depend not only upon the number of hours which he devotes to exercise, but especially upon the kind of exercise chosen. Lusk estimates that an average-sized man sleeping 8 hours, sitting 14 hours, and walking 2 hours spends about 2500 Calories; whereas if he spends 2 hours in vigorous exercise instead of walking, his total energy output rises to about 3000 Calories.

The importance of muscular activity as the chief factor governing the energy expenditure and food requirement of healthy adults calls for a careful quantitative study of its effect upon metabolism.

Quantitative relation between work performed and total metabolism. — Theoretically it is possible to determine the mechanical efficiency of a man by dividing the mechanical effect of his work by the increase of energy metabolism which the work involves. This gives the basis on which to ascertain how much extra food would be necessary to supply the energy required for the performance of any given task.

Zuntz and his associates in Berlin have carried out a long series of experiments of this kind which are described by Magnus-Levy in Von Noorden's *Metabolism and Practical Medicine.* The general bearing of these experiments may be summarized as follows:

The amount of oxygen consumed during work in excess of that during rest was regarded as a measure of that expended upon the work. As a rule the increased consumption of oxygen during work is relatively greater than the increased volume of air breathed, so that a greater proportion of the oxygen of the inspired air must be taken up by the lungs. As an example of the increase of oxygen consumption with muscular work the data obtained by Katzenstein in experiments upon the work of walking up an inclined plane may be given. The figures were as follows:

	OXYGEN CONSUMED PER MINUTE	RESPIRATORY QUOTIENT	HORIZONTAL DISTANCE	ASCENT
	cc.		Meters	Meters
At rest	263.75	0.801	—	—
Walking on very slight incline	763.00	0.805	74.48	0.58
Walking up incline with 10.8 per cent rise	1253.2	0.801	67.42	7.27

The constancy of the respiratory quotient indicates that there was no change in the nature of the material burned in the body on passing from rest to gentle, or from gentle to moderate exercise (though there is other evidence, as will be seen below, that vigorous exercise is apt to be accompanied by a rise in the respiratory quotient).

The weight moved (that of the subject and his clothing) was in this case 55.5 kilograms. From these data it was calculated that a consumption of energy equivalent to 0.223 kilogram-meter was required to move 1 kilogram of weight horizontally over a distance of 1 meter; and 2.924 kilogram-meters of energy to raise 1 kilogram through a vertical distance of 1 meter.

Experiments upon several other subjects gave similar results, indicating that these men who, while not trained in an athletic sense, were physically sound and thoroughly accustomed to this form of exercise, were able to perform 1 kilogram-meter of work in the ascent of the incline with an expenditure of only about 3 kilogram-meters of energy over that required at rest, so that the work was done with a mechanical efficiency of about 33 per cent. It is to be noted, however, that this applies only to walking done under the most favorable conditions, and not carried to the point of fatigue; also that robust men unaccustomed to this form of exercise showed efficiencies of only 20 to 25 per cent until after several days' practice, and for some subjects the maximum efficiencies found were 21 to 31 per cent.

On this basis it might be estimated that a man of average weight in walking one mile on level ground would do 8000–9000 kilogram-meters of work, or about the mechanical equivalent of 20 Calories. If this were accomplished with an efficiency of 33 per cent, it would involve an expenditure of only 60 Calories, but at an efficiency of 20 per cent 100 Calories per mile would be required.

The data of Benedict and Murschhauser's recent experiments lead to a similar conclusion. They found that the extra metabolism involved in walking at a speed of 4 miles per hour averaged 0.585 gram-calorie per kilogram-meter. For a man of 70 kilograms this would correspond to an increased energy metabolism of about 60 Calories per mile. Very fast walking (5.4 miles per hour) involved an expenditure of 0.932 gram-calorie per kilogram-meter, equivalent on the same basis to about 95 Calories per mile. To walk at a speed of nearly 5½ miles per hour required a greater expenditure of energy than to run at the same speed.

These figures may be helpful in estimating the food requirements of men who neither do active physical labor nor take vigorous exercise, yet move about more freely than in the so-called rest experiments already described. If, for example, it be assumed that a healthy man would require 2200 Calories per day when remaining in one room, and that the total additional muscular movements of a day at business and recreation were equivalent to walking five miles on level ground, his total food requirement for the day would become 2500 to 2700 Calories (36 to 39 Calories per kilogram), while activity equivalent to walking ten miles on level ground would bring the total daily requirements to 2800 to 3200 Calories (40 to 46 Calories per kilogram).

By means of the respiration calorimeter, Atwater and Benedict studied the question of mechanical efficiency with more accurate measurements of the energy involved than in the experiments of the Zuntz laboratory, but with a different form of muscular work. They placed in the calorimeter chamber an ergometer, which consisted of a fixed bicycle frame having in place of the rear wheel a metal disk which is revolved against a measured amount of electrical resistance, so that the mechanical effect of the muscular work is very accurately determined. The expenditure of energy involved in the performance of this work was estimated by comparing the total metabolism of a working day with that of the same man when living in the calorimeter chamber at rest. The average results obtained with three different men were as follows:

Subject and Nature of Experiment	Energy Transformed		Heat Equiv. of Work Performed	Mechanical Efficiency
	Total per day	Excess over that at rest		
	Calories	Calories	Calories	Per cent
Subject E. O.				
Average 13 rest experiments (42 days)	2279			
Average 3 work experiments (12 days)	3892	1613	214	13.3
Subject J. F. S.				
Average 4 rest experiments (12 days)	2119			
Average 6 work experiments (18 days)	3559	1440	233	16.2
Subject J. C. W.				
Average 1 rest experiment (4 days)	2357			
Average 14 work experiments (46 days)	5143	2786	546	19.6

With an improved ergometer of the same type as that used in the experiments just cited, Benedict and Carpenter working with J. C. W. (one of the three men above mentioned) found efficiencies ranging from 20.7 to 22.1 per cent and averaging 21.6 per cent; with other men studied, the efficiencies ranged from 18.1 to 21.2 per cent.

Benedict and Cathcart, in similar bicycle ergometer experiments in which the basis of comparison was complete rest on a couch, found efficiencies varying from 10 to 25 per cent, depending on load, speed, and the familiarity of the subject with the work, the maxima for the six men studied being 23.1, 20.4, 21.6, 22.7, 20.8, and 25.2 per cent respectively.

In another series of experiments they subtracted from the expenditure of energy during work, the amount spent when the subject, instead of lying on a couch, sat on the ergometer and allowed the pedals to be turned under his feet. Using this method of estimation they were able by careful adjustment of speed and load to realize with a professional bicycle rider an efficiency of 33 per cent or as much as Zuntz and his associates had estimated from the walking experiments.

Only under the most favorable circumstances and with subjects fully accustomed to the kind of work being performed will the actual mechanical effect produced amount to as much as one fourth to one third of the extra energy expended during work over that during rest, *i.e.* to an efficiency of 25 to 33 per cent. Not only do most occupations involve kinds of work which in their nature must be done with less efficiency than walking (or riding a stationary ergometer) but the usual hours of labor are longer than those in which the maximum mechanical efficiency is attained. The efficiency may begin to decline before any sensation of fatigue is felt.

Thus Leo Zuntz found, when he rode his bicycle for four successive hours at an average rate of 15 to 17 kilometers (about 9 miles) per hour, that he experienced no feeling of fatigue, but his determinations showed that the expenditure of energy necessary to produce a given effect had increased about 9, 13, 10, and 23 per cent at the end of 1, 2, 3, and 4 hours respectively. This is because if the same kind of work be performed for a series of hours, auxiliary muscles are gradually brought increasingly into action, partly for the performance of the work itself, partly for the fixation of the bodily framework (maintenance of posture). These auxiliary muscles work less economically than those which are used first and most naturally. For much the same reasons there is a lower efficiency in the case of work which is from the first of too fatiguing a nature because of being either excessive or unsuitably distributed. When Leo Zuntz increased his speed 2.4 times, he found his metabolism increased 4.3 times, implying a considerable loss of efficiency. Under the conditions of Benedict and Cathcart's experiments also, the efficiency was usually decreased upon increasing the speed; on the other hand a moderately heavy load was more economical than a light one.

From the data determined by Atwater and Benedict, Lusk, Becker, and their respective collaborators, it is now possible to estimate the approximate average expenditure of energy per hour under a considerable number of conditions of muscular activity. For convenience of comparison and application the original data have been reduced to a common basis of a man of 70 kilograms (154 pounds), then averaged and the average approximated to the nearest "round" number, with the results shown in the accompanying table.

ENERGY EXPENDITURE OF AVERAGE-SIZED MAN (70 KILOGRAMS) PER HOUR UNDER DIFFERENT CONDITIONS OF ACTIVITY. (APPROXIMATE AVERAGES ONLY)

Sleeping	60–70 Calories
Awake, lying still	70–85 Calories
Sitting at rest	100 Calories
Standing at rest	115 Calories
Tailoring	135 Calories
Typewriting rapidly	140 Calories
Bookbinding	170 Calories
"Light exercise" (bicycle ergometer)	170 Calories
Shoemaking	180 Calories
Walking slowly (about 2⅔ miles per hour)	200 Calories
Carpentry	240 Calories
Metal working	
Industrial painting	
"Active exercise" (bicycle ergometer)	290 Calories
Walking actively (about 3¾ miles per hour)	300 Calories
Stoneworking	400 Calories
"Severe exercise" (bicycle ergometer)	450 Calories
Sawing wood	480 Calories
Running (about 5¼ miles per hour)	500 Calories
"Very severe exercise" (bicycle ergometer)	600 Calories

By the use of these estimates the probable food requirement for a person of 70 kilograms (154 pounds) may be calculated very simply, as, for instance, in the following example:

8 hours of sleep at 65 Calories = 520 Calories
2 hours' light exercise * at 170 Calories = 340 Calories
8 hours' carpenter work at 240 Calories = 1920 Calories
6 hours' sitting at rest at 100 Calories = 600 Calories
Total food requirement for the day, 3380 Calories

Tigerstedt, in his *Textbook of Physiology*, gives estimates of food requirements for different degrees of activity as indicated by means of typical occupations, which may be useful in checking results calculated as above.

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* Going to and from work, for example.

According to Tigerstedt:

2000–2400 Calories per day suffice for a shoemaker.
2400–2700 Calories per day suffice for a weaver.
2700–3200 Calories per day suffice for a carpenter or mason.
3200–4100 Calories per day suffice for a farm laborer.
4100–5000 Calories per day suffice for an excavator.
Over 5000 Calories per day are required by a lumberman.

Lusk gives the following summary of energy requirements of women at work at typical occupations as investigated by Becker and Hamäläinen in Finland:

A seamstress sewing with a needle required 1800 Calories.

Two seamstresses, using a sewing machine, required 1900 and 2100 Calories, respectively.

Two bookbinders required 1900 and 2100 Calories.

Two household servants, employed in such occupations as cleaning windows and floors, scouring knives, forks, and spoons, scouring copper and iron pots, required 2300 to 2900 Calories.

Two washerwomen, the same servants as the last named, required 2600 and 3400 Calories in the fulfillment of their daily work.

Benedict and Cathcart find that when muscular work is severe there is a rise in the respiratory quotient, the rise being greater the more severe the work. In such cases the respiratory quotient is found to fall during the rest period following the work, and usually to a lower figure than that observed before the work was begun. They interpret this to mean that hard muscular work draws upon the stored carbohydrate of the body in slightly greater proportion than upon the stored fat. That the work is performed at the expense of both carbohydrate and fat is shown by Benedict and Cathcart's data as well as by those of many previous experiments. Apparently it is only severe muscular activity which has any appreciable influence upon the relative proportions of fat and carbohydrate burned. In the experiments cited on page 181, for example, the respiratory quotient was not changed by walking either on a horizontal surface or up an inclined plane. It should also be noted that Benedict and Cathcart found the same mechanical efficiency in work whether preceded by a carbohydrate-rich or a carbohydrate-poor diet.

Influence of Food upon Energy Metabolism

Atwater and Benedict determined directly by means of the respiration calorimeter the heat production of the same man during five fasting experiments of one to two days each, and during a four-day experiment with food about sufficient for maintenance. The average total metabolism on the fasting days was about 9 per cent lower than on the days when food was taken.

In longer fasts there may be a somewhat greater decrease in heat production. Thus, Benedict found that a man who weighed at the start 59.5 kilograms (131 pounds) metabolized, on the successive days of a seven-day fast, 1765, 1768, 1797, 1775, 1649, 1553, and 1568 Calories respectively. Naturally in long fasts factors other than the simple sparing of the direct effect of food come into play.*

Tigerstedt studied by means of the carbon and nitrogen balance the metabolism of a man who fasted for five days and for the next two days took a very liberal diet. The following data were obtained:

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* For a detailed account of the results obtained in a fasting experiment of 31 days' duration, see Benedict, *A Study of Prolonged Fasting*, Publication No. 203 of the Carnegie Institution of Washington.

	Body Weight Kilos	Calculated Total Metabolism Calories	Calories per Kilo
1st fast day	67.0	2220 *	33.2 *
2d fast day	65.7	2102 *	32.0 *
3d fast day	64.9	2024	31.2
4th fast day	64.0	1992	31.1
5th fast day	63.1	1970	31.2
Fed 4141 Calories . . .	64.0	2437	38.1
Fed 4141 Calories (2d day)	65.6	2410	36.8

These results show for man (as had previously been shown with dogs) that in fasting the total metabolism continues at a fairly constant rate in spite of the fact that the energy is obtained entirely at the expense of body material. In this case, the diet given at the end of the fasting period (4141 Calories) was approximately double what would have been required for maintenance, but the increase in energy metabolism was only 22.5 per cent over that of fasting.

The results of fasting experiments thus make it evident that the body has but little power in the direction of adjusting its energy metabolism to the energy value of its food supply.

Rubner found that each type of food exerted a more or less specific influence upon the energy metabolism, so that when the foodstuffs were fed separately, somewhat different energy values were required for the maintenance of body equilibrium. Thus, if the total metabolism of a dog fasting at 33° C. be represented by 100 Calories, he must be fed, in order to prevent loss of body substance, about 106.5 Calories of sugar, or 114.5 Calories of fat, or 140 Calories of protein. A man observed by Rubner metabolized in fasting 2042 Calories; when fed 2450 Calories in the form of sugar alone, he metabolized 2087 Calories; when

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* These figures are slightly too high because the loss of carbon on these days was due in part to combustion of glycogen, but is calculated as if due simply to protein and fat.

fed 2450 Calories in the form of meat alone, he metabolized 2566 Calories.

Recently Lusk and his coworkers have investigated the influence of the foodstuffs upon metabolism (" specific dynamic action ") very extensively and have developed the subject to such an extent that for an adequate discussion of their results the original articles[1] or Lusk's own summary[2] should be consulted. It appears from this work that when the digestion products of carbohydrate or fat are carried by the blood to the tissues the energy metabolism (rate of oxidation) rises simply because of the increased concentration of oxidizable material; but that some of the products of the digestion and intermediary metabolism of protein increase metabolism not only to a greater extent, but also in a somewhat different manner, since they seem to act as stimuli rather than merely as fuel. On an ordinary mixed diet, however, this apparent loss of energy due to eating of protein is not a very large factor in the total metabolism, since the total specific dynamic action makes the metabolism of energy for the day only about one tenth higher on a full maintenance ration than when no food is eaten.

Benedict and Roth have studied the energy metabolism of vegetarians as compared with non-vegetarians of the same height and weight in order to determine whether or not the former maintain a lower plane of basal metabolism than do people who eat meat and who are sometimes held to be unduly stimulated by the protein of their food. The energy metabolism was computed from the carbon dioxide production and oxygen consumption determined when the subjects were at complete rest and in the "post-absorptive condition," *i.e.* at least 12 hours after the last meal, the immediate specific dynamic action of the food being thus practically excluded. Under these conditions the vegetarian men and women showed average basal metabolism of 1.06 and 1.025 Calories per kilogram of body weight per hour respectively, while the corresponding data for non-vegetarian men and women were 1.10 and 1.04 Calories respectively. Benedict holds that these differences are too small to establish any essential difference in the basal energy metabolism of vegetarians and non-vegetarians of like height and weight.

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[1] Lusk. *Journal of Biological Chemistry*, Vol. 20, pages vii–xvii and 555–617. Murlin and Lusk, *Ibid.*, Vol. 22, pages 15–29.

[2] Lusk. *Science of Nutrition*, Third Edition, Chapter VII.

It is sometimes thought that superior preparation or very thorough mastication of food results in such improvement in its utilization that a material saving may be effected in the amount of food required. But it will be remembered that under average conditions only about 5 per cent of the energy value of the food is lost in digestion or expended upon the digestive process. Any improvement in those conditions through superior preparation or mastication of the food can therefore at most effect a saving of less than five per cent of the energy value. Thus the influence upon total food requirement is scarcely appreciable. The advantages of good preparation and thorough chewing of the food are very important, but they lie in other directions than reduction in the amount of food required.

Recent scientific evidence supports the view that chronic undernutrition or even simple restriction of food consumption in health, if continued sufficiently, may bring the organism to a lower level of energy metabolism than would be indicated by the weight or surface.

Regulation of Body Temperature

Climate, *season*, *housing*, *clothing*, are all factors which may influence energy metabolism through their bearing upon the regulation of body temperature.* It is evident that the maintenance of the body at a temperature above that of its ordinary environment involves a continual output of heat. This output of heat may be regulated in either of two ways: (1) By variations in the quantity of blood brought to the skin, which tend to control the loss of heat by radiation, conduction, and sweating; this is called "physical regulation." (2) By an increase in the rate of oxidation in the body in response to the stimulus of external cold; such a change in the rate of oxidation is known as "chemical regulation." The extra heat production which follows the taking of food (the specific dynamic action of the foodstuffs) may take the place of the "chemical regulation" and so help to protect the body from the necessity of burning material simply for the maintenance of its temperature. Muscular work, by increasing the production of heat in the body, may also render chemical regulation unnecessary; but apparently the specific dynamic action does not furnish energy which can be utilized for muscular work.[1]

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* For full discussion of the influence of surrounding temperature upon metabolism and the relation of metabolism to the regulation of body temperature the reader is referred to Lusk's *Science of Nutrition*.

The presence of a layer of adipose tissue under the skin as well as the custom of covering the greater part of the external surface with clothing also tends to keep down the loss of heat to the point where "physical regulation" will suffice. Lusk cites experiments by Rubner upon a man whose metabolism was determined when kept in the same cold room but with different amounts of clothing, and observes that when the man was sufficiently clothed to be comfortable the "chemical regulation" was eliminated (*Science of Nutrition*, 3d edition, page 149).

In general it seems probable that people warmly clothed and living in houses which are heated in winter are not called upon to exercise "chemical regulation" to any considerable extent; in other words, they probably do not burn any considerable amount of material merely for the production of heat, the heat required for the maintenance of body temperature being obtained in connection with the metabolism which is essential to the maintenance of the muscular tension and the various other forms of internal work. If, however, the body be exposed to cold, it may be forced to employ " chemical regulation " with a resulting increase of the food requirement, and this will occur more readily in a thin person than in one who is well protected by subcutaneous fat.

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[1] See Lusk's *Science of Nutrition*, 3d edition, pages 311-313.

The extra heat required in cold weather is probably obtained for the most part through the activities of the muscles. It is a matter of general experience that one instinctively exercises the muscles more vigorously in cold weather than in warm, and if one attempts to endure much cold without muscular exercise there results shivering — a peculiar involuntary form of muscular activity whose function appears to be to increase heat production through increasing the internal work of the body.

To a large extent, therefore, the regulation of body temperature, in case of exposure to cold, is accomplished through the activity and tension of the muscles.

The foregoing discussion has reference primarily to adults. In the case of the infant whose surface is much greater in proportion to his weight and whose muscular tone is not yet fully developed, the loss of heat to the surroundings is not so readily checked by " physical " nor so easily made good by " chemical " regulation. Unless the infant is either warmly clothed or supplied with an artificial source of heat in cold weather he may be forced to burn, for warmth, material that might better be employed for growth.

The Influence of Age and Growth

From the fact that in animals of the same species, but of different size the heat production is proportional to the surface rather than to the weight, it would follow that children must have a greater food requirement per unit of weight than adults.

In a child 2 years old weighing 25 pounds the energy metabolism is approximately half as great as in an adult of six times this weight, *i.e.* the energy expenditure per unit of weight is three times as great for the young child as for the resting man, and while for the man the expenditure may be taken as a measure of the requirement, in the case of the child an additional allowance must be made to provide the material retained in the body for growth. In studies of infants 7 to 9 months old, Rubner and Heubner found a storage of 12.2 per cent of the energy value of the food consumed, and Camerer found a storage of 15 per cent of the energy and 40 per cent of the protein of the diet.

The following data from Tigerstedt illustrate the relative intensity of metabolism at different ages:

SUBJECT	WEIGHT KGM.	METABOLISM PER DAY		
		Total Calories	Per Kgm. Calories	Per Square Meter Calories
Child, 2 weeks . . .	3.2	258	81.0	1000
Child, 10 weeks . . .	5.0	420	84.0	1200
Child, 10 years . . .	23.2	1462	63.0	1499
Man at rest'	70.0	2240	32.0	1071

According to these observations the metabolism per unit of weight is greatest in infancy and declines steadily with increasing size; but calculated per unit of surface it is distinctly less in infancy than in children of 10 years, probably because the infant sleeps a greater proportion of the time and the tension (tonus) of its muscles is not yet fully developed.

As between children and adults the energy metabolism is more nearly proportional to the surface than to the weight; but among children of about the same age the energy requirement may be computed on the basis of weight about as well as on the basis of surface.

Murlin and Bailey estimate from their own observations, and the earlier ones of Benedict and Talbot, that the energy requirement of the newborn baby *kept comfortably warm and sleeping quietly* may be placed tentatively between 1.7 and 2.0 Calories per kilogram per hour, the lower figure for a very fat (10 lb.) child and the higher for a thin (6 lb.) child. According to these authors even vigorous crying does not raise this figure more than 40 per cent. Benedict and Talbot in their later publication [1] give measurements of minimum heat production of 94 newborn infants (2 hours to 6 days old) which range from 1.33 to 2.17 Calories, averaging 1.75 Calories per kilogram per hour. " Maximum " energy metabolism, chiefly due to vigorous crying, was also observed in 93 of these cases and found to average 65 per cent above the resting value, while in several instances (10 out of 93) " crying and extreme restlessness " resulted in energy expenditure more than double that of the same infant at rest.

With the development of the musculature and of muscular tonus, the energy expenditure of the normal infant increases for a time even more rapidly than his body weight, so that at from 2 months to 1 year of age the expenditure of energy *while sleeping* averages 2.7 Calories per kilogram per hour (average of Howland's, Benedict and Talbot's, and Murlin and Hoobler's data as summarized by the latter). During the waking hours the rate of expenditure is of course materially higher, and in calculating food requirements allowance must be made for growth and for the possibility of losses through imperfect utilization of the food. In order to provide adequately for all contingencies and support the rapid growth which is normal at this age, it is estimated that a vigorous child will require during the greater part of the first year about 100 Calories of food per kilogram of his body weight per day. But in cases of artificial feeding, since the digestive tract must be gradually educated to handle the milk of a different species, it will often be necessary to feed much less than 100 Calories per kilogram per day at first, perhaps for several months, and only very gradually increase the food allowance.

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[1] *Physiology of the New Born Infant*, Publication No. 233, Carnegie Institution of Washington, 1915.

From the end of the first year until growth is completed the food requirement increases, but not so rapidly as does the body weight, so that while the allowance of food becomes larger per day it becomes smaller per kilogram. On the latter basis the energy requirement at the different ages may be estimated approximately as follows:

Under 1 year	100 Calories per kilogram	(45 Calories per lb.)
1– 2 years	100–90 Calories per kilogram	(45–40 Calories per lb.)
2– 5 years	90–80 Calories per kilogram	(40–36 Calories per lb.)
6– 9 years	80–70 Calories per kilogram	(36–32 Calories per lb.)
10–13 years	75–60 Calories per kilogram	(34–27 Calories per lb.)
14–17 years	65–50 Calories per kilogram	(30–22 Calories per lb.)
18–25 years	55–40 Calories per kilogram	(25–18 Calories per lb.)

Children who are very active or growing very rapidly may require even more food than the table just given suggests. Such cases are perhaps most frequently found among boys between 10 and 15 years of age. DuBois finds in boys 12 and 13 years old an average *basal* metabolism (complete rest and almost complete fasting) of 1.76 Calories per kilogram per hour, or about 75 per cent above that of healthy adults.* Assuming average activity for boys of this age the energy expenditure during 24 hours would probably amount to 60 to 70 Calories per kilogram and as this is a period of rapid growth the *requirement* would be materially higher than the rate of expenditure.

Assuming average size at the different ages the allowances in Calories per day become about as follows:†

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* Per unit of surface the basal energy metabolism of these boys was about 25 per cent higher than that of healthy men.

† See also the more detailed table of energy allowances for children in Chapter XIV.

Children	of 1– 2 years inclusive . .	1000–1200 Calories per day
Children	of 2– 5 years inclusive . .	1200–1500 Calories per day
Children	of 6– 9 years inclusive . .	1400–2000 Calories per day
Girls	of 10–13 years inclusive . .	1800–2400 Calories per day
Boys	of 10–13 years inclusive . .	2300–3000 Calories per day
Girls	of 14–17 years inclusive . .	2200–2600 Calories per day
Boys	of 14–17 years inclusive . .	2800–4000 Calories per day

In estimating the food requirement of a family it is usually preferable to consider each child's energy requirement directly rather than to count the children as equivalent to fractions of the hypothetical "average man."

Above the age of 17 years, although there is still some growth, differences in activity due to occupation become so great that the food requirement will usually depend as much upon occupation as upon age.

The fuel value of children's dietaries should always be liberal in order to provide amply for muscular activity and for a more intense general metabolism than that of the adult. Furthermore, throughout the period of growth the food must supply a certain amount of material to be added to the body in the form of new tissue in addition to all that which is oxidized to support metabolism.

Age	Height		Weight		Food Requirement without Muscular Labor	
Years	Meters	Feet and inches	Kilos	Lbs.	Total per day Calories	Per. Kgm. per day Calories
1	0.70	2:3	10	22	1000	100
5	1.00	3:3	17	37	1400	82
10	1.28	4:2	26	57	1800	70
15	—	—	50	110	2800	56
20	1.71	5:7 +	65	143	3000	46
30	1.72	5:8 −	69	152	2750	40
40	1.71	5:7 +	70	154	2500	36
60	—	—	68	150	2300	34
70	—	—	65	143	2000	31
80	—	—	63	139	1750	28

With the elderly, on the other hand, the intensity of metabolism is diminished and the body not only needs less food, but has less ability to deal with excess, so that the food requirement gradually declines and may become 10 or 20 per cent, or possibly even 30 per cent, lower than in middle life.

In the table on page 197 are given the estimated height, weight, and food requirement of an average man at different ages, the figures for height and weight being based upon the data given by Hill for males of the Anglo-Saxon and Teutonic races (*Recent Advances in Physiology and Biochemistry*, page 284).

These estimates of food requirements are intended to represent approximate averages of available data and to allow for such exercise as would naturally be taken at the age, exclusive of anything which would ordinarily be considered physical labor. They thus illustrate in an approximate way the rate at which the amount of food required for healthy maintenance per unit of body weight declines from infancy to old age.

DuBois has recently published in graphic form his estimates of the basal energy metabolism per unit of body surface at different ages. The graph is reproduced by Lusk (*Science of Nutrition*, 3d edition, page 128).

The average basal metabolism, per unit of surface, found by DuBois in boys of 12 to 13, in men, and in women was as follows:

AVERAGE BASAL METABOLISM OF BOYS, MEN, AND WOMEN (DUBOIS)

SUBJECTS	AGE IN YEARS	CALORIES PER HOUR PER SQUARE METER	
		Computed according to Meeh's formula	Computed by DuBois height-weight formula
Boys	12–13	45.7	49.9
Men	20–50	34.7	39.7
Women	20–50	32.3	36.9
Men	50–60	30.8	35.2
Women	50–60	28.7	32.7
Men	77–83	—	35.1

Influence of sex. — Whether sex shall be said to influence the energy requirement will depend upon our use of terms. Boys spend on the average more energy than girls, and men more than women, but it is doubtful if the differences are due to other causes than have been considered above. In experiments in which children were allowed to move about in a small respiration room, boys were found to expend decidedly more energy than girls of the same age and weight; but this was probably due to the greater restlessness and muscular tension of the boys, for in another series in which both boys and girls were kept motionless and relaxed during the observations the difference was not found. Benedict and Emmes found, as noted above, a slightly higher basal metabolism in men than in women of the same height and weight, but attribute this to a difference in the average composition of the body.

While sex alone seems not to be a measurable factor in energy metabolism, the performance of the reproductive functions may make large demands upon the maternal organism. As weight increases during pregnancy energy metabolism increases in at least equal proportion. In the last two weeks of human pregnancy Murlin finds the energy metabolism *per unit of weight* about 4 per cent higher than for non-pregnant women. During lactation, when the entire nutritive requirement of the nursing infant is being met through the mother, the energy needs of the latter are greatly increased. Production of milk involves an extra energy requirement much beyond the actual energy value of the milk secreted. While accurate determinations are not at hand, it seems safe to conclude that the nursing mother taking only moderate exercise may need as much food as a man at muscular work. Liberal feeding of the nursing mother (*e.g.* up to 2800 to 3000 Calories for a woman with moderate muscular exercise) is not only important for the conservation of her own bodily resources but may prolong the period of lactation and thus be of great value to the child as well.[1]

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[1] For general discussion of the problem of maintaining breast feeding, see papers by Sedgwick, Abt, and Hoobler in the *Journal of the American Medical Association* for Aug. 11, 1917 (Vol. 69, pages 417–428).

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CHAPTER VIII

FACTORS DETERMINING THE PROTEIN REQUIREMENT

ANIMAL cells under all conditions of life are constantly breaking down proteins into simpler substances which the body eliminates. Since this breaking down or "catabolism" of protein does not stop either in fasting or under the most liberal feeding with fats and carbohydrates, it follows that there is always a need for protein whatever the supply of other food.

Protein metabolism differs widely from energy metabolism in the conditions which determine its amount, for protein metabolism is governed mainly by the kind and amount of food, and to only a slight extent if at all by muscular exercise; whereas energy metabolism is governed mainly by the muscular exercise, and to only a relatively small extent by the food. By giving food rich in fats and carbohydrates but poor in protein, the protein metabolism of a healthy man can easily be brought to less than 50 grams per day, and then by changing to a diet rich in protein, it may be increased to 150 or even 200 grams per day; *i.e.* the rate of protein metabolism can be increased 200 to 300 per cent in a few days by a change in diet alone, all other conditions remaining the same.

Protein Metabolism in Fasting

Since the diet has such a great influence upon the amount of protein metabolized, it might be expected that the basal protein metabolism could be observed best in fasting. But in fasting the energy metabolism of the body is only a little lower than with food; the amount of combustion continues nearly the same although only body material is available; and since the body must consume so much of its own substance to obtain the energy needed, there is always a chance that in fasting some protein may be burned simply as fuel. Accordingly the protein metabolism in fasting may be greater than that which represents the needs of the body when properly fed, while on the other hand it may be abnormally low through the effort of the body to adjust itself to the abnormal condition.

The amount of protein broken down in fasting is much influenced (1) by the previous habit as regards protein consumption, and (2) by the metabolism of stored glycogen and stored fat.

The direct effect of the level of protein metabolism on the days preceding the fast is shown in the following data obtained by Voit in experiments upon a dog weighing 35 kilograms:

INFLUENCE OF PREVIOUS DIET ON NITROGEN ELIMINATION IN FASTING (VOIT)

	FOODS OF PRECEDING DAYS AND GRAMS OF UREA PER DAY		
	Meat 2500 grams	Meat 1500 grams	Bread
Last day with food	180.8	110.8	24.7
First day of fasting	60.1	29.7	19.6
Second day of fasting	24.9	18.2	15.6
Third day of fasting	19.1	17.5	14.9
Fourth day of fasting	17.3	14.9	13.2
Fifth day of fasting	12.3	14.2	12.7
Sixth day of fasting	13.3	13.0	13.0

The influence of the metabolism of the previously stored glycogen upon the amount of protein metabolized in fasting is well illustrated by the following three experiments with one individual:[1]

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[1] Benedict, *Influence of Inanition on Metabolism.* Carnegie Institution of Washington (1907).

EXPERIMENT	FIRST DAY OF FASTING		SECOND DAY OF FASTING	
	Glycogen metabolized	Nitrogen eliminated	Glycogen metabolized	Nitrogen eliminated
	grams	*grams*	*grams*	*grams*
I	181.6	5.84	29.7	11.04
II	135.3	10.29	18.1	11.97
III	64.9	12.24	23.1	12.45

It will be seen that the nitrogen output was less when there was available for metabolism a considerable supply of previously stored glycogen. Since most of the stored glycogen is used up on the first day of fasting, its influence upon the protein metabolism is short-lived as compared with that of the stored fat.

The influence of the available supply of body fat upon the protein metabolism of fasting is shown by the following observations of Falck, on the protein metabolism of two fasting dogs — the one lean, the other fat:

FALCK'S LEAN DOG		FALCK'S FAT DOG	
Fasting days	Grams protein catabolized per day	Fasting days	Grams protein catabolized per day
1–4	26.1	1–6	29.9
5–8	24.6	7–12	26.7
9–12	33.9	13–18	26.1
13–16	38.0	19–24	22.3
17–20	31.9	25–29	20.0
21–24	3.9	30–34	16.8
On the 25th day the dog died.		35–38	15.7
		40–44	13.0
		45–50	13.6
		55–60	12.2
		Dog still healthy after 60 days.	

A rise in protein metabolism of the lean dog after the 8th day showed that from this time he used protein largely as fuel — so largely that the results were fatal in 25 days of fasting. The fat dog, having plenty of other fuel in the form of fat, used protein to a much smaller extent, so that he was able gradually to accommodate himself to a lower level of protein metabolism and to endure a fast of 60 days' duration.

The professional faster, Succi, starting with a good store of body fat, fasted 30 days* with the following results:

Five days on ordinary food . . .	101.4 grams protein per day
1– 5th days fasting	80.4 grams protein per day
6–10th days fasting	53.1 grams protein per day
11–15th days fasting	36.2 grams protein per day
16–20th days fasting	33.1 grams protein per day
21–25th days fasting	29.3 grams protein per day
26–30th days fasting	33.3 grams protein per day

Since Succi's health remained good throughout his fast, it might be thought that the true protein requirement of his body was not greater than the smallest figure found for any period — in this case about 30 grams per day. On the other hand, it may well be supposed that, since the body increases its protein metabolism to an abnormally high rate under influence of excessive protein feeding, so under the influence of fasting the body may be able to adjust itself to an abnormally low rate of protein metabolism; and the fact that the protein metabolism continues to diminish for such a long time in fasting gives weight to the supposition that the body is here gradually adapting itself to an abnormal condition. One might assume that in some particular period of Succi's fast, the effect of previous feeding might no longer be apparent and the conditions had not yet become abnormal as the result of the fasting, in which case the expenditure of protein during one of these periods would represent his normal requirement. Any such assumption must, however, be more or less arbitrary. A much more definite idea of the normal dietary need is obtained by determining experimentally how much protein must be contained in the daily food in order to keep the body in protein (or nitrogen) equilibrium.

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* The output of nitrogen and of several other elements during a 31-day fast recently described by Benedict may be found in Chapter IX.

Nitrogen Balance Experiments and the Tendency toward Equilibrium at Different Levels of Protein Intake

The estimation of the nitrogen balance has already been referred to as one factor in the determination of the total food requirement by means of metabolism experiments; and it has been shown that the balance may be found either by comparing the total intake with the total output, or by comparing the amount absorbed with the amount catabolized and eliminated through the kidneys.* When intake exceeds output, there is a plus balance which indicates a storage of nitrogen and therefore of protein in the body; a minus balance (greater output than intake) indicates a loss of body protein. When the balance is 0, or so near 0 as to be within the limits of experimental error, the body is said to be *in nitrogen (or protein) equilibrium.*

The healthy full-grown body tends to establish nitrogen equilibrium by adjusting its rate of protein metabolism to its food supply within wide limits. The time required by the body for this adjustment depends mainly upon the extent to which the diet is changed.

The following observations by Von Noorden illustrate the establishment of equilibrium after only moderate changes in the diet:

A young woman weighing 58 kilograms (128 pounds) at rest in bed was given food furnishing protein, 106 grams; fat, 71.6 grams; carbohydrate, 200 grams; fuel value, 1860 Calories per day.

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* Theoretically the elimination through the skin should also be determined and included in the calculation; practically this is usually neglected unless on account of warm weather or vigorous exercise the subject has perspired profusely. For data on nitrogen in perspiration see Benedict, *Journal of Biological Chemistry,* Vol. 1, page 263 (1906) and *A Study of Prolonged Fasting,* Publication No. 203 of the Carnegie Institution of Washington, pages 233–235.

EXAMPLE OF ADJUSTMENT TO DIMINISHED INTAKE

Total nitrogen of food	16.96 grams
Lost in digestion (nitrogen in feces)	.94 gram
"Absorbed"	16.02 grams

	NITROGEN CATABOLIZED AND ELIMINATED THROUGH KIDNEYS	NITROGEN BALANCE
	grams	*grams*
1st day	18.2	− 2.18
2d day	17.0	− 0.98
3d day	15.8	+ 0.22
4th day	16.0	+ 0.02
5th day	15.7	+ 0.32

Here there was practical equilibrium after the second day. The small amount of nitrogen represented as stored on the third, fourth, and fifth days was very likely lost through the skin. This was a case of adjustment to a lowered protein intake, for the food previously taken, although not accurately observed, was known to have been rich in protein.

Another experiment was made by Von Noorden with the same patient to show the time required to reach equilibrium after increasing the intake of protein. In this case the food furnished 2030 Calories per day and the nitrogen balance was as follows:

EXAMPLE OF ADJUSTMENT TO INCREASED INTAKE

DAY	NITROGEN IN FOOD	NITROGEN IN FECES	NITROGEN "ABSORBED"	NITROGEN CATABOLIZED	NITROGEN BALANCE
	grams	*gram*	*grams*	*grams*	*grams*
1	14.40	0.70	13.70	13.60	+ 0.10
2	14.40	0.70	13.70	13.80	− 0.10
3	14.40	0.70	13.70	13.60	+ 0.10
4	20.96	0.82	20.14	16.80	+ 3.34
5	20.96	0.82	20.14	18.20	+ 1.94
6	20.96	0.82	20.14	19.50	+ 0.64
7	20.96	0.82	20.14	20.00	+ 0.14

Here where the amount of protein fed was increased from 90 to 130 grams without change in the total fuel value of the diet, the body reached equilibrium on the fourth day after the increase.

It is apparent therefore:

(1) That the body tends to adjust its protein metabolism to its protein supply.

(2) That when the body is accustomed to a certain rate of protein metabolism, it requires an appreciable length of time to adjust itself to a materially higher or lower rate.

Hence the rate of protein metabolism on any given day will depend in part upon the rate of metabolism to which the body has been accustomed and in part upon the protein intake for the day. When the protein supply varies from day to day, the metabolism for each day is influenced by both the factors, with the net result that the elimination equals the intake when averaged for a sufficiently long period, although the data for any particular day might show a distinct gain or loss. When the protein supply is constant for a few days, the effect of previous habit usually disappears and equilibrium is established as in the above cases.

A transitory loss of nitrogen from the body is apt to be due simply to the taking of less than the usual amount of protein food, but a persistent loss indicates that the diet is insufficient, either in total food (calories) or in protein, to enable the usual adjustment to take place.

A transitory storage of nitrogen in the body may occur as the result of an increase either of the protein or of the total fuel value of the food; but a persistent storage occurs, as Von Noorden has pointed out, only under the following conditions:

(1) In the growing body (or in pregnancy) where new tissue is being constructed.

(2) In cases where increased muscular exercise calls for enlargement of the muscles.

(3) In cases where, owing to previous insufficient feeding or to wasting disease, the protein content of the body has been more or less diminished and consequently any surplus available is utilized to make good the loss.

Protein-sparing Action of Carbohydrates and Fats

It has been shown above that, in fasting experiments, the amount of stored glycogen and fat in the body exerts a " sparing " influence upon protein metabolism, the amount of protein catabolized being smaller when the supplies of glycogen and fat are more abundant. Similarly the amounts of carbohydrates and fats in the food influence the rate of protein metabolism as indicated by the nitrogen excretion. The loss of protein which occurs on an insufficient diet may be diminished or even stopped by adding carbohydrates or fat to the food; and if carbohydrate or fat be added to the diet of a man in nitrogen equilibrium, there results a temporary decrease in nitrogen output with a corresponding storage of protein in the body. The former observation could be interpreted as meaning simply that the body draws upon its stored protein for energy so long, and only so long, as the fuel value of the food is insufficient; but the fact that addition of carbohydrate or fat to a diet already sufficient may cause an actual storage of protein indicates that the " protein-sparing action " or " protein-protecting power " of carbohydrates and fats involves something more than merely the question whether the body " needs " to burn its stored protein as fuel.

As this is a matter of great importance, it may be well to consider somewhat carefully (1) the experimental evidence, and (2) the theoretical explanations, regarding the protein-sparing action of the carbohydrates and fats. For an account of the earlier experiments on this subject, especially those of Voit and Rubner upon dogs, the reader is referred to Lusk's *Elements of the Science of Nutrition*. Only some of the more important of the experiments upon men can be described here.

Lusk,[1] experimenting upon himself, showed the susceptibility of the protein metabolism to the sudden withdrawal of carbohydrate food. In one experiment a liberal mixed diet containing 20.55 grams of nitrogen was taken until the body was nearly in nitrogen equilibrium, and then, without any other change, 350 grams of carbohydrate were withdrawn from the daily food. On the first day the body protein was largely protected by the carbohydrate previously stored in the body in the form of glycogen, but on the second day the nitrogen metabolism had risen from 19.84 to 27.00 grams per day. In another experiment, upon a diet containing less protein, withdrawal of carbohydrate increased the nitrogen excretion from 11.44 to 17.18 grams per day.

In these cases, as in the fasting experiments, the loss of body protein was less in those subjects having a good store of body fat than in those which were thin.

Kayser compared the efficiency of carbohydrates and fats as sparers of protein by observing the effect upon the nitrogen balance of replacing the carbohydrates of the food by such an amount of fat as would furnish the same number of calories, and then after three days resuming the original diet. This experiment and that of Tallquist which follows are given somewhat fully, as they illustrate well the methods and results of investigations based mainly upon the question of nitrogen equilibrium. The observer, who served as his own subject, was twenty-three years old, of good physique, with a small store of body fat, and weighed 67 kilograms. In the first and third periods he ate meat, rice, butter, cakes, sugar, oil, vinegar, and salad. In the second period the diet was changed so as to consist of meat, eggs, oil, vinegar, and salad, so that practically all the carbohydrate was withdrawn and replaced by fat. The two diets had practically the same fuel value and protein content. The results of this experiment are shown in the following table:

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[1] *Zeitschrift für Biologie*, Vol. 27, page 459 (1890).

NITROGEN BALANCE WHEN FEEDING ISODYNAMIC QUANTITIES OF CARBOHYDRATE AND FAT (KAYSER)

DAY	INTAKE				OUTPUT	NITROGEN BALANCE
	Total nitrogen	Fat	Carbohydrates	Fuel value	Total nitrogen	
	grams	*grams*	*grams*	*Calories*	*grams*	*grams*
1	21.15	71.1	338.2	2590	18.66	+ 2.46
2	21.15	71.8	338.2	2596	20.04	+ 1.11
3	21.15	71.8	338.2	2596	20.59	+ 0.56
4	21.31	71.8	338.2	2600	21.31	± 0.00
5	21.51	221.1	000.0	2607	23.28	− 1.77
6	21.55	217.0	000.0	2570	24.03	− 2.48
7	21.55	215.5	000.0	2556	26.53	− 4.98
8	21.10	70.4	338.2	2581	21.65	− 0.55
9	21.10	70.4	338.2	2581	19.20	+ 1.89
10	21.10	70.4	338.2	2581	19.65	+ 1.45

It is evident from the nitrogen balance of the first period that the amount of protein in the food was here greater than necessary, but that equilibrium was fully established in four days. On substituting fat for carbohydrate there is a marked increase of protein catabolism with corresponding loss of nitrogen from the body, and what is especially noteworthy, there was no evidence of any tendency to regain equilibrium during this period, but on the contrary the loss of nitrogen became greater each day the fat diet was continued; whereas, upon returning to the mixed diet, not only was the loss of protein stopped, but the body almost at once began replacing the protein it had lost, although the nitrogen and calories of the food were practically unchanged.

Tallquist[1] compared the protein-protecting powers of isodynamic amounts (amounts having equal energy value) of carbohydrates and fats when only a part of either was replaced by the other. The subject was Tallquist himself, a man twenty-eight years old, in good health, and weighing about 80 kilograms. The experiment was performed in Rubner's laboratory, and the diet contained such an amount of total food as was estimated by Rubner to be just about sufficient to supply the energy requirements of the body, viz., 36 Calories per kilogram per day. The experiment covered 8 days divided into two equal periods. In the first four-day period the diet was rich in carbohydrates, in the second period it was rich in fats. An excellent feature of this experiment is that there was no change in the nature of the protein fed. All foods furnishing any significant amount of nitrogen were the same in the two periods of the experiment.

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[1] *Archiv für Hygiene*, Vol. 41, page 177.

The food of the first period consisted of meat, milk, butter, bread, sugar, coffee, beer. That of the second period contained the same amounts of meat, milk, bread, coffee, and beer, but less sugar, more butter, and some bacon. The same amount of salt was taken in each case. The principal data of the experiment may be summarized as follows:

Nitrogen Balance when Feeding Isodynamic Quantities of Carbohydrate and Fat (Tallquist)

Day	Intake					Output	Nitrogen Balance
	Total nitrogen	Fat	Carbohydrates	Alcohol	Fuel value	Nitrogen	
	grams	*grams*	*grams*	*grams*	*Calories*	*grams*	
1	16.27	44.0	466	18.5	2867	17.11	− 0.84
2	16.27	44.0	466	18.5	2867	14.40	+ 1.86
3	16.27	44.0	466	18.5	2867	14.65	+ 1.62
4	16.27	44.0	466	18.5	2867	15.58	+ 0.69
5	16.08	140.0	250	19.0	2873	17.66	− 1.58
6	16.08	140.0	250	19.0	2873	17.32	− 1.24
7	16.08	140.0	250	19.0	2873	15.94	+ 0.14
8	16.08	140.0	250	19.0	2873	16.22	− 0.14

Here only a part of the carbohydrate, about half of that present, and an amount representing about one third of the total fuel value of the diet, was replaced by fat. The change evidently had an unfavorable influence upon the nitrogen balance but the loss of body protein was relatively small and continued only 2 days.

Atwater[1] compared the protein-sparing action of carbohydrate and fat in experiments in which the subject, an athletic young man of 76 kilos, performed a considerable amount of work. The experiments were carried out in the respiration calorimeter and covered in all 15 experimental days upon a diet rich in carbohydrates, arranged in four periods which were alternated with four equal periods in which the diet was rich in fats. The change from carbohydrate to fat and vice versa involved about 2000 Calories or nearly half the fuel value of the diet. The average results per day for the entire series of experiments were as follows:

	On Diet Rich in Carbohydrates	On Diet Rich in Fat
Available Calories in food	4532	4524
Heat equivalent of work performed, Calories	558	554
Nitrogen in food, grams	17.5	17.1
Nitrogen in feces, grams	2.5	1.7
Nitrogen in urine, grams	16.6	18.1
Nitrogen balance, grams	− 1.6	− 2.7

Here again there is a difference in favor of the carbohydrate, but one which is so small as to be of almost no practical significance.

It appears that the carbohydrate of the food cannot be entirely replaced by an equal number of calories in the form of fat without an unfavorable effect upon the nitrogen balance; but that when the replacement is such as to affect not over one half of the total calories, the difference in protein-sparing action is but slight. Ordinarily on a normal mixed diet the same number of calories has about the same protein-sparing effect.

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[1] *Ergebnisse der Physiologie*, Vol. 3, Part I, page 497.

Landergren [1] also found that it is only when the carbohydrate of the diet is entirely replaced by fat that the comparison is so strikingly against the fat as it seemed to be in Kayser's experiment. In Landergren's experiments the condition studied was not one of approximate equilibrium, but rather of nitrogen hunger. He fed men diets of adequate fuel value but containing only about one gram of nitrogen daily, and found that by four days of such feeding the urinary nitrogen may be reduced to about 4 grams per day. In one experiment in which the daily food contained 750 grams of carbohydrates the urine of the fourth day showed 3.76 grams of nitrogen. The carbohydrate was then entirely replaced by fat, with the result that the following days' urines contained respectively 4.28, 8.86, and 9.64 grams of nitrogen. Evidently in the case of a man accustomed to feeding largely upon carbohydrates the complete replacement of carbohydrate by fat leads to a loss (or an increased loss) of body protein. But by subsequent experiments of the same series it was found that a diet containing nearly half its calories in carbohydrate, and nearly half in fat, had apparently the same protein-sparing power as one made up almost exclusively of carbohydrates.

The explanation offered by Landergren is that when the diet supplies no carbohydrate, the glycogen of the body soon becomes exhausted, and the carbohydrate needed to keep up the constant glucose content of the blood is obtained largely by the breaking down of proteins.

This might suffice to explain the difference in effect of carbohydrate and fat, but not the fact that addition of a non-nitrogenous nutrient to a diet already sufficient may cause storage of nitrogen in the body.*

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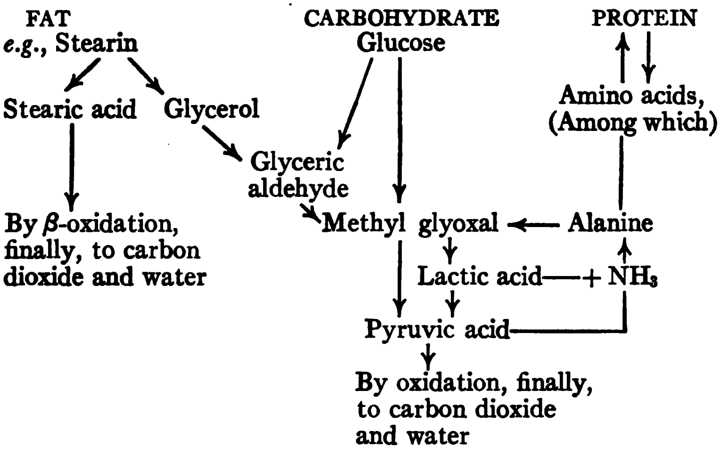
[1] *Skandinavisches Archiv für Physiologie*, Vol. 14, page 112 (1903); Abstract Experiment Station Record, Vol. 14, page 1099.

A satisfactory explanation of both sets of facts appears to be afforded by the recent advances in our knowledge of the fate of foodstuffs in metabolism which were outlined in Chapter V. The outstanding relationships of the three groups of foodstuffs in the intermediary metabolism may be indicated schematically as follows:


FAT
e.g., Stearin
Stearic acid
Glycerol
By β-oxidation, finally, to carbon dioxide and water
CARBOHYDRATE
Glucose
Glyceric aldehyde
Methyl glyoxal
Lactic acid
Pyruvic acid
By oxidation, finally, to carbon dioxide and water
PROTEIN
Amino acids, (Among which)
Alanine
+ NH_3

Since ammonia is always being formed in protein catabolism (by deaminization of amino acids), and since the ammonium salts of α-ketonic acids, such as pyruvic acid, are convertible into amino acids which are building materials for body protein, we have here a mechanism by which an intermediary product of carbohydrate metabolism (pyruvic acid) takes up a " waste product " of protein metabolism (ammonia) and turns it back into amino acid again. Thus carbohydrate, in undergoing metabolism, " spares " protein, not only by serving as fuel so that protein need not be drawn upon for this purpose, but also by furnishing material which in combination with ammonia (otherwise a waste product) can actually be converted in the body into some of the amino acids of which body proteins are composed and with which they are in equilibrium. This explains how an increased intake of carbohydrate, with resulting increase of pyruvic acid, naturally leads to increased synthesis of amino acids and thus to a tendency toward protein storage, or, to express the same thing in somewhat different terms, tends to push the reaction, Amino acids $\rightleftarrows$ Protein, toward the right.

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* Furthermore Lusk points out that Landergren's explanation is hardly adequate to cover the results obtained in gelatin-feeding experiments.

According to present theory, most, if not all, of the energy of the carbohydrate becomes available through oxidation processes which involve the intermediate production of pyruvic acid, an α-ketonic acid whose ammonium salt is capable of conversion into amino acid. Of the fat only the glyceryl radicle (about one twentieth of the fuel value) is oxidized through pyruvic acid, while the fatty acid radicles, representing about nineteen twentieths of the energy of the fat, are metabolized through β-oxidation processes which yield, so far as we know, no product whose ammonium salt is convertible into amino acid in the body. Hence complete withdrawal of carbohydrate, even though substituted by sufficient fat to yield an equal number of calories, must be expected to result in increased excretion of nitrogen; but when no more than half of the carbohydrate is replaced by fat there seems to be enough pyruvic acid produced to meet the practical requirements of economical metabolism of protein.

Protein Requirement in Normal Nutrition

From what has been said above it will be apparent that, within rather wide limits, the greater the amounts of carbohydrates and fats eaten, the smaller will be the amount of protein required to maintain nitrogen equilibrium.

For practical purposes, however, we may eliminate the question of the extent to which protein metabolism can be restricted by the use of excessive amounts of other food and reduce the problem to this: When the total food is properly adjusted to the size and activity of the subject so that there is sufficient but not excessive fuel to meet all the energy requirements, how much protein must the daily food contain in order to keep the body in nitrogen equilibrium?

The most extended investigation on the protein requirement of man is that of Chittenden.* The general plan followed in this investigation was to have each man reduce his protein food gradually without any great change in his other habits. This gradual reduction of the protein intake was continued usually for some weeks, sometimes for several months, before any comparison of intake and output was attempted. During this preliminary period upon a restricted diet there was in almost every case a loss of weight, and from previous observations † under similar conditions we may safely assume that there was a considerable loss of body protein. After a sufficient period of adjustment there was usually a tendency for the body weight and the rate of protein metabolism (measured by the amount of nitrogen eliminated through the kidneys) to become fairly constant, indicating that the body had adapted itself to the new conditions. When this point had been reached, a nitrogen balance experiment was made, the intake and output being determined by weighing and analyzing for nitrogen all food consumed and all nitrogenous material given off from the body except that in the perspiration. The fuel value of the food consumed during the same period was calculated by means of figures taken from standard tables. From these calculated fuel values it would appear that the energy of food consumed by Chittenden's subjects was in general about equal to the usual estimates of the energy requirements for similar occupations, though in several specific instances the subject may have unduly restricted his total food intake and thus created an energy deficit and a tendency toward negative nitrogen balance.

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* See Chittenden's *Physiological Economy in Nutrition* and *Nutrition of Man*.

† Neumann, for example, in 35 days on insufficient diet lost 96 grams of nitrogen corresponding to 600 grams of protein, equivalent to about 2.5 kilograms (5.5 pounds) of muscle tissue.

Chittenden bases his estimate of the protein requirement, not only upon the nitrogen balances, but also upon the amounts of nitrogen observed to be eliminated daily through the kidneys over long periods in which the body may or may not have been in complete equilibrium, but in which health and efficiency were certainly maintained. The first men to serve as subjects in this investigation were Chittenden himself and his associates, who all continued their professional work and either reported no effect or felt benefited by the change to the low protein diet. Similar experiments were then made upon a squad of soldiers, who during the test were quartered near the laboratory and were given regular exercise in the gymnasium in addition to light duties about their quarters. These men showed marked improvement in physical condition during the test, probably due in part to their more regular habits of life and their gymnastic exercises. In order to eliminate this latter factor while still applying the low protein diet to young and physically active men, the investigation was extended to cover a group of university athletes who were already well-trained and in prime physical condition at the beginning of their dietary experiment. These athletes not only maintained, but in many cases improved, their gymnastic records while on the low protein diet, one of them winning an all-round gymnastic championship during the time. Chittenden states[1] that his data "are seemingly harmonious in indicating that the physiological needs of the body are fully met by a metabolism of protein matter equal to an exchange of 0.10 to 0.12 gram of nitrogen per kilogram of body weight per day, provided a sufficient amount of non-nitrogenous foods is taken to meet the energy requirements of the body." This would correspond to 44 to 53 grams of protein per day for a man of average weight (70 kilograms, 154 pounds, without clothing), and Chittenden considers that for such a man an allowance of 60 grams of protein per day should certainly be entirely adequate.

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[1] *Nutrition of Man*, pages 226, 272.

In a recent examination of the available literature upon this subject there were found 86 experiments upon adults showing no abnormality of digestion or health, in which the diet was sufficiently well adjusted to the probable requirement and the nitrogen balance showed sufficient approach to equilibrium to make it appear that the total output of nitrogen might be taken as an indication of the protein requirement. These experiments are taken from 20 independent investigations in which 41 different individuals (37 men and 4 women) served as subjects. For purposes of comparison the daily output of total nitrogen in each experiment was calculated to protein and this to a basis of 70 kilograms of body weight. Reckoned in this way, the apparent protein requirement as indicated by the data of individual experiments ranged between the extremes of 20.0 and 79.2 grams, averaging 49.2 grams of protein per man of 70 kilograms per day. Thus the average falls well within the range of Chittenden's estimate of the amount of protein required for normal nutrition when the energy value of the diet is adequate.

Examination of the data recorded in the original papers indicates that the wide differences in amounts of protein catabolized in the different experiments cannot be attributed primarily to the kind of protein consumed nor to the use of diets of fuel values widely different from the energy requirements. Apparently the most influential factor was the extent to which the subject had become accustomed to a low protein diet.

Difference between Minimum Requirement and Standard Allowance of Protein

It may be well to point out here the distinction between the amount of protein actually required on the one hand, and, on the other hand, the amount which it may be thought best to allow in the planning of dietaries. The term "requirement" should preferably be applied only to the former; the latter would better be called the protein allowance or the standard for protein. The difference between the amount actually required and the amount which would ordinarily be allowed in planning a dietary is much greater with protein than with fuel value. Surplus fuel is stored as fat, and if excessive fatness is to be avoided, the fuel value of the food must not greatly exceed the energy requirements of the body; but surplus nitrogen is rapidly eliminated from the body and, so long as no injury to health results, leaves no evidence of having been taken in excess of body needs. The eating of a considerable surplus of protein has become habitual, and such a surplus of protein in the food is believed by many people to constitute a desirable "factor of safety," if not indeed to exert a directly beneficial effect upon health and stamina. Hence there is a tendency to set the protein allowance or standard for protein considerably higher than the actual requirement.

If the average daily food requirement of a man at rest be taken as 2000 Calories including 50 grams of protein, the same man at work may require 3000 or 4000 Calories while his actual requirement for protein will not be appreciably increased. If the protein be held at 50 grams while the food is increased from 2000 to 3000 to 4000 Calories, the protein in percentage of total calories would be in the three cases 10 per cent, 7 per cent, and 5 per cent respectively. Thus it is plain that when the energy requirement is subjected to considerable variations by differences in muscular activity, the protein requirement cannot be taken as constituting a fixed proportion of the total calories, since muscular work increases the energy requirement very greatly and the protein requirement very little if at all. In practice, however, a diet of 2000 Calories would usually contain somewhat over 50 grams of protein; and when the man increased his activity and his total food consumption, he would probably increase his protein intake in almost the same proportion, for he would in most cases simply eat a larger quantity of his usual kind of food.

Moreover, those differences in food requirement which are due to differences in age and size will usually affect the energy requirement and the protein requirement in about the same proportion; and, as the majority of dietaries are planned for family groups, the differences in age and size are usually quite as important as the differences in muscular activity. Thus there is rational basis for the custom of allowing enough protein to furnish from 10 to 15 per cent of the total energy value of the diet.

Influence of the Choice of Food

When isolated proteins are fed singly, striking differences in nutritive value appear, as has been shown in Chapter III. In view of this fact it may seem strange that in the experiments hitherto conducted to determine the protein requirement of man the kind of protein fed has not exerted a more striking influence upon the results obtained. There is, however, no real discrepancy between the two sets of findings. The experiments described in Chapter III were for the purpose of comparing individual proteins isolated even from the other proteins which always accompany them in natural or commercial food materials, and were conducted largely upon rapidly growing young animals, in which there is an active synthesis and retention of protein, so that a deficiency in the supply of any amino acid which is required in the construction of body protein is apt to be quickly and plainly reflected in a diminution or cessation of growth. On the other hand, in experiments like those described in the preceding section, where the purpose is not to compare proteins but to measure the normal protein requirement, the diet is naturally made up, not of isolated proteins or even of single or unusual foods, but (ordinarily at least) of such combinations of staple foods as is believed to represent a normal diet, so that even a relatively simple ration arranged for the purposes of such an experiment would probably contain a number of different proteins among which any peculiarities of amino acid make-up would be apt to offset each other. Moreover the experiments of the latter group have been made entirely upon adults whose protein requirement was limited to that of maintenance. In such cases there is no longer a demand for amino acids to be built into new tissue, but only to maintain the equilibrium which now exists between amino acids and proteins in the tissues already full grown. Any of the amino acids whose radicles are contained in tissue proteins may be expected to contribute something to the maintenance of such an equilibrium, whereas there can be no growth unless all the necessary amino acids are present. In a corresponding series of experiments upon growing children or nursing mothers the influence of food selection would probably be much more pronounced.

Even for the maintenance of adults protein requirement may be found to be considerably influenced by food selection when experiments suitably planned to test the question are carried out. The inadequacy of gelatin as a sole protein food and its inferiority to meat or milk protein when substituted beyond a certain proportion are well known. A series of experiments, designed to demonstrate differences in nutritive efficiency for man of the protein supplied by different staple articles of food, was carried out by Karl Thomas in Rubner's laboratory and the striking results obtained have been widely quoted, often on Rubner's authority. These results, however, have as yet failed of confirmation, and on some important points have been so directly refuted by later workers using longer experimental periods, as to make it appear that Thomas's plan of experimenting and mode of interpretation were not entirely suited to the solution of the question at issue.

Thomas[1] thought he had demonstrated that meat protein was greatly superior to bread or potato protein for the maintenance of body tissue; but Hindhede finds no such difference, being able to maintain normal nutrition with either bread or potato nitrogen in relatively small amounts.

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[1] Thomas, *Archiv für Anatomie und Physiologie*, 1909, pages 219–302.

Rose and Cooper * have also demonstrated the high value of potato nitrogen in the maintenance of nitrogen equilibrium, and preliminary experiments in the writer's laboratory † have tended to confirm Hindhede's finding that nitrogen equilibrium may be maintained on a relatively low intake of protein in the form of bread.

Of greater practical importance than the experiments with bread alone are those † which show the maintenance of nitrogen equilibrium over long periods on low protein diets in which bread is the chief source of protein, but is supplemented by small amounts of milk.

Since estimates of protein requirement, in order to be of general application, should provide for the needs of growth, reproduction, and lactation, as well as for maintenance, it will be well to consider more fully the results obtained in feeding experimental animals upon known rations throughout the period of growth or the entire life cycle.

It will be remembered that Osborne and Mendel, feeding isolated proteins in liberal proportion (18 per cent) in diets adequate and well balanced as regards all other factors, found that edestin, a typical vegetable globulin, was able to supply all the protein requirements of maintenance, reproduction, and growth, even through three generations of rats. With gliadin as the sole protein, maintenance was satisfactory but growth was inhibited; but an addition of lysine to this diet caused an immediate resumption of growth. When the supply of lysine was cut off, growth again ceased. A ration containing zein as the sole protein did not suffice even for maintenance; but when tryptophane was added to it, or gliadin, which contains tryptophane, it served to maintain body weight, and on further addition of lysine, growth ensued.

In order to emphasize such differences as these it is sometimes thought advantageous to classify proteins as:

A. Complete: Capable of maintaining adults and providing for normal growth of the young when used as a sole protein

* Rose and Cooper, *Journal of Biological Chemistry*, Vol. 30, pages 201–204.

† Not yet published.

food. Casein and lactalbumin of milk; ovalbumin and ovovitellin of egg; glycinin of soy bean; excelsin of Brazil nut; edestin, glutenin, and maize-glutelin of the cereal grains.

B. Partially Incomplete: Capable of maintaining life but not of supporting normal growth. Gliadin of wheat is the well-demonstrated example of this class.

C. Incomplete: Incapable either of maintaining life or of supporting growth, when fed as the sole protein. Zein of corn (maize), and gelatin are the conspicuous examples.

Any such grouping of the proteins, however, must be used with much discrimination, and with great care to insure an understanding of the quantitative aspects of the experimental data, if misconceptions are to be avoided. Edestin is a conspicuous example of a "complete" protein, having served as above noted as the sole protein food of a family of rats for three generations; but when the percentage of edestin in the food mixture was considerably reduced, results like those above described for gliadin were obtained — the diet did not support a normal rate of growth, but this could be secured by adding lysine to the food mixture. Similarly casein when fed in reduced proportion to the total food mixture did not support normal growth; but growth became normal when cystine was added. Thus "complete" proteins may behave as "partially incomplete" when fed in reduced proportion. It is also to be remembered that varying rates of growth in different species (not to mention other differences) make inadmissible any broad generalizations as to the proportion in which any protein should be fed to species other than that with which its "completeness" or "incompleteness" has been demonstrated.

In some of their most recently published experiments (1916) Osborne and Mendel give quantitative measurements of the relative efficiency (for support of growth in young rats) of some of the "complete" proteins. The rate of gain obtained with 8 per cent of lactalbumin required 12 per cent of casein or 15 per cent of edestin; or, as they also state the result, " to produce the same gain in body weight 50 per cent more casein than lactalbumin was required, and of edestin nearly 90 per cent more." In maintenance experiments, 2.4 to 3 per cent of lactalbumin was as effective as 3.5 to 4 per cent of casein or edestin.

On extending their experiments from rats to chicks, Osborne and Mendel again found that proteins rich in lysine are much more effective for growth than those in which the proportion of lysine is much smaller.

McCollum found milk protein much more efficient than wheat or maize protein in supporting the growth of young pigs.

As in growth, so in lactation, the demand for material for the construction of new protein creates a condition in which differences of value in the protein fed may readily become more apparent than when only maintenance is involved. Hart and Humphrey find that in meeting the protein requirements of milch cows, milk protein and the protein of flaxseed, " oil meal," are about 50 per cent more efficient than the proteins of the corn (maize) or of the wheat kernel; and Hoobler has shown that milk is the best form of food protein for the production of human milk and the protection of the body protein of the nursing mother.

Influence of Muscular Exercise

At one time it was supposed that muscular power was generated at the expense of muscle substance and this, of course, necessitated the belief that muscular work always increased protein metabolism. Since we now know that the muscles work quite as well at the expense of carbohydrates and fats as of protein, the conclusion that muscular work necessarily increases the metabolism of protein is far from inevitable. It is only necessary to observe the effects of regular muscular exercise, either in athletic training or in normal labor, to see that the muscles do not waste away when thus used, but rather tend to become larger. Such a growth of the muscles tends toward a storage rather than a loss of protein. Usually, however, muscular work also results in increased appetite, and it is difficult to separate the effects of the exercise from those of the extra food.

Whether muscular work acts directly to increase the amount of protein metabolized in the body can only be determined by experiments in which sufficient extra fats and carbohydrates are fed to furnish the extra fuel required on the working days. But since fats and carbohydrates spare protein, the feeding of these in any excess over just what is necessary to provide for the increased energy requirement would tend to decrease the metabolism of protein and counteract any effect which the muscular work might otherwise have in increasing protein metabolism. Hence, in order to show conclusively whether muscular work of itself has any influence upon the protein metabolism, it would be necessary to determine the mechanical efficiency of the man, then to bring him into equilibrium with an amount of food just sufficient for his needs, and finally to have him perform a measured amount of work at the same time adding to his diet an amount of fats and carbohydrates just sufficient to furnish the extra energy required for the work performed. Such elaborate experiments have not yet been made, but we have sufficient data to show that they are not necessary for practical purposes. Many experiments have shown conclusively that increased work, when accompanied by a sufficient increase in the amount of fats and carbohydrates fed, does not necessarily increase the metabolism of protein.

The following data from Atwater (*Report of the Storrs, Connecticut, Agricultural Experiment Station for 1902–1903*, page 127) show the average results of a long series of rest and work experiments with men in the respiration calorimeter:

MUSCULAR WORK AND PROTEIN METABOLISM (ATWATER)

NATURE OF EXPERIMENT	AVERAGE METABOLISM PER DAY					
	PER PERSON		PER KILOGRAM BODY WEIGHT		PER SQUARE METER SURFACE	
	Energy, Calories	Protein, Grams	Energy, Calories	Protein, Grams	Energy, Calories	Protein, Grams
Rest: Food generally sufficient for equilibrium; 5 subjects, 27 experiments, covering 82 days	2310	103.8	33.5	1.51	1116	50.1
Work: 8 hours per day. Food generally not quite sufficient for equilibrium; 3 subjects, 24 experiments, covering 76 days	4556	108.1	62.9	1.49	2129	50.5

Comparing the figures either per unit of weight or of surface, it will be seen that muscular work sufficient to nearly double the energy metabolism had no appreciable effect upon the amount of protein metabolized. Considering the large amount of exceptionally accurate research represented in these figures, they seem to justify the conclusion that if muscular work has any tendency to increase the "wear and tear" of muscle substance, such effect is normally balanced by the tendency of the muscles to grow (and therefore store protein) when exercised.

Moreover, it is certain that any effect which muscular work might possibly have in increasing protein metabolism would be incomparably less than its effect in increasing the total metabolism. If, then, starting with a diet which maintains protein equilibrium at rest, the total food is increased sufficiently to provide for the muscular work, and the increase in the diet is accomplished by adding any reasonable combination of food materials, we may feel sure that these will supply plenty of protein to meet any possible increase in the protein requirement. Hence, in planning the diet of a man at hard muscular work, any reasonable combination of foodstuffs given in sufficient abundance to meet the energy requirement will almost certainly supply an ample amount of protein.

Shaffer has studied the output of ammonia, creatinine, and uric acid as well as of total nitrogen during rest and work and finds no significant change in any of these. Lusk considers it fully proved that neither the amount nor the character of protein metabolism is changed by muscular activity.

Protein Requirement in Relation to Age and Growth

If a man at moderately active work takes a diet which furnishes 3000 Calories and 75 grams of protein, he is taking 10 per cent of his calories in the form of protein. Of course the protein requirement cannot bear a fixed relation to the calorie requirement, since the latter is largely influenced by activity, while the former is not. Most men, when at complete rest, would require more than 10 per cent of their calories in the form of protein because the lack of exercise would not reduce the protein requirement to the same extent as the energy requirement. On the other hand, most Americans are accustomed to take more than 10 per cent of their calories as protein regardless of whether they require it or not. If, then, the active man's need for protein is met by supplying him with 10 per cent of his needed calories in the form of protein, this will serve as a convenient starting point in considering the requirements of a child. Let this be compared with the normal dietary of an infant. Human milk averages about 1.6 per cent protein, 4.0 per cent fat, 7.0 per cent carbohydrate. Here about 9 per cent of the calories are taken in the form of protein, or about the same proportion as has been allowed for the full-grown active man. Furthermore Hoobler has shown experimentally that this is as high a proportion of protein as the infant will utilize with the highest efficiency in growth of body tissue. During the suckling period the growth is relatively more rapid than at any other age. Mendel * gives the following figures:

The Relative Daily Gain in Body Weight of Children

In the first month is about	1.00 per cent
At the middle of the first year	0.30 per cent
At the end of the first year	0.15 per cent
At the fifth year	0.03 per cent
Maximum in later years	
for boys	0.07 per cent
for girls	0.04 per cent

If, then, the full-grown man and the child at the time of most rapid growth each requires but 10 per cent of his calories in the form of protein, it seems probable that this proportion is also sufficient for any intermediate age, if the diet is of ample fuel value, and the protein is of the right kind. But the proper selection of the protein is of very great importance in the feeding of children, who differ from most other young mammals in that their period of growth is so many times longer than the suckling period. Even the child that is nursed for a year and attains three times his birth-weight before weaning will still have much the greater part (probably five sixths) of his growth to make on other food. By the time growth is complete he will probably have about twenty times the body weight and more than twenty times the body protein with which he was born.

Growth at the normal rapid rate of early childhood involves the conversion of a very considerable part, sometimes as much as one third, of the protein of the food into body protein. This can be accomplished to the best advantage only when (1) the protein of the food is largely of the kind most efficient in supporting growth, *i.e.* milk protein; (2) the protein is well "protected" by the protein-sparing action of liberal amounts of carbohydrate and fat.

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* *Childhood and Growth*, p. 18.

That the child needs a diet of high fuel value to meet the requirements of his energy metabolism has already been pointed out (Chapter VII). It is because the high protein requirement of childhood (for young children more than twice as much per unit of weight as for adults) is paralleled by an equally high energy requirement that the diet of the child need not contain a higher percentage of its calories in the form of protein than does the ordinary diet of the adult, if the protein for the child is well chosen.

Usually, however, a well-planned dietary for a child will show a somewhat more than average proportion of its calories in the form of protein because after weaning the main feature of the child's diet should be cows' milk which furnishes about 19 per cent of its calories in the form of protein. A child, fed mainly upon cows' milk and taking enough food to amply cover his energy requirement, will therefore receive a safe surplus of protein in the best available form. With a full quart of milk in the daily dietary of the growing child the other foods may be selected chiefly with reference to other qualities than their protein content; without a liberal use of milk the proper feeding of a growing child becomes a very difficult problem.

Having discussed the protein requirements of ordinary adult maintenance and of growth, the requirements of the aged should also be considered. This does not require extended discussion, since advancing age involves no new features but only a gradual modification of those pertaining to middle life.

In general, elderly people show a somewhat diminished protein requirement and likewise a diminished power of dealing with excess. Surplus protein taken in the food is not so rapidly absorbed and catabolized, and, while there appears to be no essential difference in the form in which the nitrogen is finally excreted, the susceptibility to excessive putrefaction of protein appears to be increased. It would seem that in the dietary of the aged the protein should be reduced to at least as great an extent as are the calories.

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CHAPTER IX

INORGANIC FOODSTUFFS AND THE MINERAL METABOLISM

The Elementary Composition of the Body

From various estimates by different writers the average elementary composition of the human body may be presumed to be approximately as follows:

Oxygen, about	65. per cent
Carbon, about	18. per cent
Hydrogen, about	10. per cent
Nitrogen, about	3. per cent
Calcium, about	2. per cent
Phosphorus, about	1. per cent
Potassium, about	0.35 per cent
Sulphur, about	0.25 per cent
Sodium, about	0.15 per cent
Chlorine, about	0.15 per cent
Magnesium, about	0.05 per cent
Iron, about	0.004 per cent
Iodine Fluorine Silicon	Very minute quantities

Traces of some other elements such as manganese and aluminium may perhaps be normal constituents of the body also, and even arsenic has been discussed as a possible essential element. In this book only those elements are discussed of which the amounts concerned in daily metabolism can be measured quantitatively by present methods.

Since all of the substances in the body are continually undergoing disintegration and renewal, it follows that there must be a constant metabolism or exchange of every element which enters into body structure. More or less of each element must each day be metabolized and eliminated; and, if equilibrium is to be maintained, an equal amount must be supplied.

Simple proteins furnish only five of the fifteen chemical elements which are known to be essential to human nutrition, while fats and carbohydrates are composed of but three of these five. Ten of the fifteen essential elements, or seven of the twelve which are essential in amounts sufficiently large to be measurable by present methods, must therefore be furnished by some ingredients of the intake other than simple proteins, fats, and carbohydrates. These same elements are found to remain either wholly or largely in the ash of food materials when the latter are burned in the air; and when the food is metabolized in the body they are excreted chiefly in the form of mineral matter. These elements are therefore grouped as " ash constituents," " minerals," " mineral salts," " inorganic elements," or " the inorganic foodstuffs "; and their metabolism is commonly designated as " the mineral metabolism." None of these terms is entirely appropriate. To designate the elements which remain in the ash when food is burned as ash constituents is accurate but not very instructive, since the materials of which a food ash is composed may have existed in quite different forms of combination in the food before it was burned. The terms " mineral " and " inorganic " are likely to be somewhat misleading. Some of the elements (as sodium and chlorine) do exist in the food and enter and leave the body in inorganic forms; others (as iron and sulphur) exist in the food and function in nutrition as essential constituents of organic matter and become inorganic only as the organic matter is oxidized, *i.e.* only in the late stages of their metabolism; still others (as phosphorus) are supplied to the body by the food in both organic and inorganic forms.

The elements concerned in " the mineral metabolism " may exist in the body and take part in its functions in at least three kinds of ways:

(1) As bone constituents, giving rigidity and relative permanence to the skeletal tissues.

(2) As essential elements of the organic compounds which are the chief solid constituents of the soft tissues (muscles, blood cells, etc.).

(3) As soluble salts (electrolytes) held in solution in the fluids of the body, giving these fluids their characteristic influence upon the elasticity and irritability of muscle and nerve, supplying the material for the acidity or alkalinity of the digestive juices and other secretions, and yet maintaining the neutrality or slight alkalescence of the internal fluids as well as their osmotic pressure and solvent power.

A man under average conditions of diet, activity, and health usually excretes daily from 20 to 30 grams of mineral salts, consisting essentially of chlorides, sulphates, and phosphates of sodium, potassium, magnesium, and calcium (as well as ammonium salts from the protein metabolism).

The purpose of this chapter and the one following is to sketch briefly the metabolism of these substances, with a more detailed quantitative study of the three elements (calcium, phosphorus, and iron) which assume an especial prominence in the practical problems of nutrition.

Metabolism of Chlorides — Use of Common Salt

Except for the hydrochloric acid of the gastric juice, practically all the chlorine involved in metabolism enters, exists in, and leaves the body in the form of chlorides — much the greater part as sodium chloride. The amount of sodium chloride which is ordinarily added to food as a condiment is so large that the amounts of sodium and chlorine present in the various foods in the fresh state become of little practical consequence. Among animals the herbivora require salt while the carnivora do not, the latter obtaining sufficient salt for their needs from the flesh, and more especially from the blood, of their prey.

Sodium occurs, chiefly as chloride, abundantly in the blood and other fluids of the animal body and in much lower concentration in the tissues. Potassium, on the other hand, occurs to a greater extent as phosphate than as chloride. It is most abundant in the soft solid tissues — in the corpuscles of the blood, the protoplasm of the muscles, and other organs, and also in the highly specialized fluids which some of the glandular organs secrete, notably in milk. Since the cells are in constant contact with the circulating fluids, the abundance of potassium in the cells and of sodium in the fluids makes it evident that the taking up of salts by the cells is an active or "selective" process. A conspicuous function of the salts in the tissues is the maintenance of the normal osmotic pressure, but solutions of different salts of equal osmotic pressure are by no means interchangeable, and it is not possible to replace successfully the potassium in the cell by an equivalent amount of sodium.

There seems to be a relation between the taking up of salt and the retention of water in the tissues. The effect of decreasing the salt in the diet is to decrease the quantity of salt in the tissues, and at the same time their water content. An explanation of this lies in the fact that, since body tissues and fluids must maintain a constant concentration of sodium chloride, a reduction in the absolute quantity of salt must result in a corresponding reduction in the quantity of water present.

Attention is frequently called to the fact that sodium chloride is the only salt which we seem to crave in greater quantities than occur naturally in our food, and that we share this appetite with the herbivorous animals. Bunge holds that this is because a high intake of potassium (as in most vegetable foods) tends to increase sodium elimination. Bunge tested this theory upon his own person by taking 18 grams of potash (as phosphate and citrate) in one day. This increased the elimination of sodium chloride by 6 grams.

In his *Physiological and Pathological Chemistry* (Chapter VII), Bunge records extended and interesting observations and discussion upon the relation of diet to the craving for salt, and concludes that while one might live without the addition of salt to the food even on a diet largely vegetarian, yet without salt we should have a strong disinclination to eat much of the vegetables rich in potassium, such as potatoes. " The use of salt enables us to employ a greater variety of the earth's products as food than we could do without it." But also, according to Bunge: " We are accustomed to take far too much salt with our viands. Salt is not only an aliment, it is also a condiment, and easily lends itself, as all such things do, to abuse." While Bunge's explanations may not be entirely adequate in detail, there seems to be little doubt as to the correctness of his main deductions.

Since the sodium chloride taken with the food passes through the body and is excreted by the kidneys without undergoing any chemical change, the rate of excretion quickly adapts itself to the rate of intake within wide variations.

When no chloride is taken, the rate of excretion falls rapidly to a point where the daily loss is only a very small fraction of the amount ordinarily consumed and excreted. Thus in an experiment by Goodall and Joslin * in which a healthy man was placed upon a diet adequate in protein and energy value but practically free from salt, the excretion of chlorine on each of 13 successive days was respectively: 4.60, 2.52, 1.88, 0.87, 0.69, 0.48, 0.46, 0.40, 0.26, 0.22, 0.22, 0.17, 0.17 grams.

Cetti in ten days of fasting excreted all together 13.13 grams, and Belli in ten days on a diet poor in salt lost 11.8 grams of sodium chloride. In Benedict's recent study of prolonged fasting * his subject lost 8.44 grams of chlorine (equivalent to 13.93 grams sodium chloride) during the first ten days, 2.13 grams chlorine during the second ten days, and 1.57 grams chlorine during the third ten days of the fast. (The detailed data may be found on a later page.) Since the body is supposed to contain about 100 grams of sodium chloride, it will be seen that even when there was complete deprivation of salt for ten to thirty days, the total losses did not exceed 10 to 20 per cent of the amount estimated as usually present in the body. The salt thus readily given off by the body has been regarded by some as a measure of the excess which the body has been forced to carry in consequence of the extravagant amounts of salt which are commonly taken with the food. Magnus-Levy, however, thinks that the reduced amount of sodium chloride left in the body after such a loss is " not a physiological optimum, but rather a physiological minimum."

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* Goodall and Joslin, *Transactions of the Association of American Physicians*, Vol. 23, page 92 (1908).

Moderate variations in the amount of salt taken have no significant effect upon metabolism. Large amounts increase the quantity of protein catabolized, and, through overstimulating the digestive tract, may also interfere with the absorption and utilization of the food.

Metabolism of Sulphur

Plants absorb sulphates from the soil and use the sulphur in the synthesis of proteins. Minute quantities of inorganic sulphates may be taken by man in food and drink, but by far the greater part of the sulphur concerned in metabolism enters the body in organic combination and, so far as known, chiefly as protein. The metabolism of sulphur is therefore a part of the protein metabolism, and in many respects the metabolism of sulphur tends to run parallel with that of nitrogen. In a series of ten experiments (each of 3 to 5 days' duration) upon

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* Benedict, Publication No. 203, Carnegie Institution of Washington.

man,* in which the food consisted of bread and milk in varying amounts and proportions, the percentage absorption from the digestive tract was nearly the same for the sulphur as for the nitrogen of the food, and the excretion of the end products ran so closely parallel that in every case in which the body stored nitrogen it also stored sulphur, and vice versa.†

It is well known that individual proteins show relatively much greater differences in sulphur than in nitrogen content, so the ratio of nitrogen to sulphur varies widely, as is shown by the following examples selected from the data for pure proteins compiled by Osborne:

Kind of Protein	Nitrogen Per Cent	Sulphur Per Cent	Ratio of Nitrogen to Sulphur
Legumin	18.04	0.385	46.9 : 1
Zein	16.13	0.600	26.9 : 1
Edestin	18.69	0.88	21.2 : 1
Gliadin	17.66	1.027	17.2 : 1
Leucosin	16.80	1.280	13.1 : 1
Casein	15.78	0.80	19.7 : 1
Myosin	16.67	1.27	13.1 : 1
Serum globulin	15.85	1.11	14.3 : 1
Egg albumin	15.51	1.616	9.6 : 1

Thus, while many proteins approximate the usually assumed average of 16 per cent nitrogen and 1 per cent sulphur, there are considerable deviations from this ratio in both directions.

Under ordinary conditions, however, no protein is eaten in a pure state, but only as the material containing it is used as an article of food. It is therefore the proportion of sulphur to the total protein of the food which determines the ratio of sulphur to nitrogen available for nutrition.

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* Bulletin 121, Office of Experiment Stations, U. S. Department of Agriculture.

† Exceptions to such parallelism of nitrogen and sulphur balances have, however, been reported in certain pathological conditions.

The proportion of sulphur to total protein has been determined in most staple foods, of which the following are representative: *

FOOD MATERIAL	SULPHUR IN PERCENTAGE OF TOTAL PROTEIN
Lean beef	0.95–1.00
Eggs	1.4
Milk	0.95–1.09
Wheat flour, crackers	1.15–1.29
Entire wheat	1.30
Oatmeal	1.55
Beans	0.69–1.00
Peas	0.80–0.94
Potatoes	1.07

Taking these figures as typical, it would appear that in those staple foods which contribute the greater part of the protein of the diet, the ratio of protein to sulphur does not differ greatly, and that in most cases of ordinary mixed diet there would be consumed not far from 1 gram of sulphur in each 100 grams of protein. We may therefore expect that in health and on an ordinary diet the sulphur requirement will usually be covered when the protein supply is adequate.

When proteins (or their cleavage products) are oxidized in the body, the sulphur becomes converted for the most part into sulphuric acid, which, of course, must be neutralized as rapidly as it is formed. The greater part of the sulphuric acid formed in metabolism appears in the urine as inorganic sulphates; a smaller part is found combined with organic radicles in the form commonly known as "ethereal" or "conjugated" sulphates. The amount of ethereal sulphate or the ratio of ethereal to inorganic sulphate is quite variable, depending mainly upon the

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* In the data here given, nitrogen and sulphur were determined in the same specimens. Average percentages of protein and sulphur in nearly all important food materials may be found in Tables I and II, respectively, of the Appendix.

amount and character of the intestinal putrefaction, which in turn is apt to be considerably influenced by the food. On ordinary mixed diet about one tenth or one twelfth of the sulphate sulphur in the urine ordinarily appears as ethereal sulphates; but when the meat in the diet is replaced by milk, the putrefaction is usually lessened and the proportion of ethereal sulphates lowered. In one case of a healthy man who had been on a bread and milk diet for a week, only one thirtieth of the sulphate sulphur was in the form of ethereal sulphates.

Not all of the metabolized sulphur is eliminated as mineral or " ethereal " sulphate; a part is given off in less completely oxidized forms. This " unoxidized " or " neutral " sulphur usually constitutes in healthy persons on full diet from 5 to 15 per cent of the total sulphur eliminated. In Folin's experiment upon very low protein diet, although the total sulphur metabolism was markedly decreased, the quantity of neutral sulphur excreted remained about constant, so that the relative proportion of sulphur appearing in this form was increased.

Metabolism of Phosphorus

Phosphorus compounds are as widely distributed in the body and as strictly essential to every living cell as are proteins.

Phosphates are constantly excreted from the body even after long fasting. During a fast the rate of excretion of phosphates does not fall off rapidly like that of chlorides, but tends to run more nearly parallel with the nitrogen excretion, as would be expected in view of the fact that the phosphates of the urine represent not only an excretion of preëxistent salts, but also the result of the metabolism of body tissue.

Some of the relations of the phosphorus compounds to nutritional functions are outlined by Forbes and Keith as follows:

" Among the several inorganic elements involved in animal life phosphorus is of especial interest. No other one enters into such a diversity of compounds and plays an important part in so many functions. Structurally, it is important as a constituent of every cell nucleus and so of all cellular structures; it is also prominent in the skeleton, in milk, in sexual elements, glandular tissue, and the nervous system. Functionally, it is involved in all cell multiplication, in the activation and control of enzyme actions, in the maintenance of neutrality in the organism, in the conduct of nerve stimuli, and through its relation to osmotic pressure, surface tension, and imbibation of water by colloids it has to do with the movement of liquids, with the maintenance of proper liquid contents of the tissues, with cell movements, and with absorption and secretion" (Ohio Agricultural Experiment Station, Technical Bulletin No. 5, page 11).

While the phosphorus compounds of the body and of the food are very numerous and might be classified differently according to the standpoint from which they are being considered, it will be convenient for our present purposes to divide them into four main groups:

1. Inorganic phosphates, of which potassium phosphate is probably the most abundant in food and in the fluids and soft tissues of the body, while calcium phosphate is the chief inorganic constituent of bones.

2. Phosphorus-containing proteins, including the nucleoproteins of cell nuclei, the lecitho-proteins, and the true phosphoproteins such as casein or caseinogen of milk and ovovitellin of egg yolk.

3. Phosphatids, phospholipins or phosphorized fats — including lecithins, lecithans, kephalins, etc. — which occur in large quantity in brain and nerve tissue and in smaller concentration (but probably as essential components) in all the cells and tissues of the body, not only of man, but of plants and animals generally. The phosphatids are therefore widely distributed in food materials, but are found in extremely varying proportions in foods of different types. Egg yolks are conspicuously rich

in phosphatids, about two thirds of the phosphorus of the egg being present in this form.

4. Phosphoric acid esters of carbohydrates and related substances such as inositol ("inosite") and the natural salts of such esters. The calcium, magnesium, and potassium salts of "phytic acid," * collectively known as phytates, phytins, or phytin, have for some years been regarded as the most abundant phosphorus compounds of the wheat kernel and probably of the grains and legumes generally, if not of all vegetable foods. Recent investigations indicate, however, that not all the phosphorus compounds which were supposed to be phytins are really salts of phytic acid. As has been explained in Chapter I, the recent work of Northrup and Nelson indicates that starch contains phosphorus as an essential constituent, and there are other indications of phosphorus-containing carbohydrates or carbohydrate-phosphoric acid esters in food materials and also of the formation of hexose-phosphoric acid esters in the body in the course of the carbohydrate metabolism.

Thus we may think of the phosphorus with which we have to deal in food and nutrition as being partly in the form of inorganic phosphates and partly in combination with (or present as a constituent of) each of the three groups of organic foodstuffs — proteins, fats, and carbohydrates, or closely related substances.

In the course of digestion and metabolism the phosphoric acid radicles are split off from the organic radicles and ultimately nearly all of the phosphorus leaves the body as inorganic phosphate. To what extent the cleavage of the organic phosphorus compounds occurs in the digestive tract under ordinary conditions and to what extent, if at all, the phosphorus of phosphoproteins or phosphatids, for example, is absorbed in organic form is still a subject of investigation.

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* Phytic acid is probably inositol-hexa-orthophosphoric acid, $C_6H_{24}O_{24}P_6$ (Robinson and Mueller).

Interrelations of Phosphates, Phosphoproteins, and Phosphatids

Phosphates, nucleoproteins, and phosphatids are all prominent as body constituents.

The insoluble phosphates constitute the chief mineral matter of bone; while soluble phosphates are essential constituents of the blood and protoplasm. It is largely to the presence of the phosphates that the blood and protoplasm owe their ability to remain neutral or faintly alkaline, notwithstanding the constant production of acid in metabolism, as will be seen in connection with the discussion of the maintenance of neutrality below.

The nucleoproteins as constituents of cell nuclei and the phosphatids as prominent constituents of brain and nerve tissue and as less prominent but doubtless essential components of the tissues generally have functions distinct from each other and from the phosphates. On the assumption of a more active metabolism in the cell nuclei or in the brain and nerve tissue than in the bones, there has sometimes been a tendency to regard fluctuations of phosphorus output as indicative of increased or decreased metabolism of nucleoproteins or phosphatids. It is probable, however, that the eliminated phosphorus represents more largely material which has functioned as phosphate. One reason for this is that the bones contain so large a share of the total phosphorus of the body. According to Voit's estimate, a man's skeleton contains about 600 grams of phosphorus; his muscles, about 56 grams; his brain and nerves, about 5 grams. With the bones in possession of such a predominant share of the body phosphorus, it would seem that the metabolism of bone tissue, even though relatively inactive, must exert a considerable influence upon the phosphorus output. Moreover, the soluble phosphates of the blood and protoplasm are constantly tending to be eliminated from the body (through the kidneys or the intestinal walls or both) and perhaps increasingly so in proportion as they become changed into acid phosphates in the performance of their function of maintaining neutrality by reacting with the acids produced in metabolism. Before taking up the quantitative study of the phosphorus requirement we must consider the nutritive relations of the different types of phosphorus compounds, and whether these are sufficiently interchangeable in nutritive function so that one may properly speak of phosphorus requirement, simply, without discriminating between phosphates, phytates, phosphoproteins, and phosphatids.

Such experimental evidence as is cited here will be given in general in chronological order, to indicate, if possible, how present views have actually developed, and to suggest that they may at any time require modification as a result of further research.

Meischer studied the formation of complex from simpler phosphorus compounds in the adult animal body by observations upon the Rhine salmon, which during the breeding season remain a long time in fresh water, taking no food, but developing large masses of roe and milt at the expense of muscular tissue. This process evidently involves the formation of considerable amounts of nucleoproteins and phosphatids from simpler proteins, fats, and phosphorus compounds of the muscles. Paton [*] has studied the salmon of Scotland with similar results. Is there then any advantage in feeding phosphorus in organic forms?

Marcuse,[†] followed by Steinitz,[‡] Zadik,[§] and Leipziger,[||] studied, by metabolism experiments on dogs, the nutritive value of phosphoproteins, when fed to the exclusion of phosphates and when contrasted with equivalent amounts of phosphorus and nitrogen fed in the form of mixtures of inorganic phosphates and simple proteins. Casein and ovovitellin were taken as typical phosphoproteins and compared with either myosin or edestin fed with inorganic phosphates. Rohmann * summarized the results as a whole and found a striking difference in the phosphorus balances in favor of the phosphoproteins as against the mixtures of simple proteins with inorganic phosphates. The storage of nitrogen was also more pronounced in the periods in which the phosphorized proteins were fed. The results appear to justify Rohmann's conclusion that the nutritive values of phosphorized and phosphorus-free proteins are not entirely the same, the former being especially adapted to furnish the material for tissue growth.

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[*] *Journal of Physiology*, Vol. 22, page 333.

[†] *Archiv für die gesammte Physiologie* (Pflüger), Vol. 67, page 373.

[‡] *Ibid.*, Vol. 72, page 75.

[§] *Ibid.*, Vol. 77, page 1.

[||] *Ibid.*, Vol. 78, page 402.

In experiments upon men, Ehrstrom † and Gumpert ‡ have found that a smaller amount of phosphorus will maintain phosphorus equilibrium when taken in the form of casein than when taken largely as dicalcium phosphate or as meat, the phosphorus of which is largely in the form of potassium phosphate. On the other hand Keller § in a study of the phosphorus metabolism of young children found evidence that storage of phosphorus was favored by food (like milk) which contained a liberal supply of phosphates in addition to the organic phosphorus compounds; and Von Wendt found that the loss of phosphorus occurring on a diet very poor in ash could be greatly reduced by the addition of dicalcium phosphate to the food.

In cow's milk the greater part of the phosphorus appears to exist as phosphate, but there can be no doubt that the milk phosphorus as a whole is available for the needs of the young of the species, especially in view of the parallelism pointed out by Bunge and Abderhalden between the phosphorus and calcium content of milk and the rate of growth of the young. (See accompanying table.)

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* *Berlin klinische Wochenschrift*, Vol. 35, page 789.

† *Skandinavisches Archiv für Physiologie*, Vol. 14, page 82.

‡ *Medische Klinik*, Vol. 1, page 1037.

§ *Archiv für Kinderheilkunde*, Vol. 29, page 1.

SPECIES	NO. OF DAYS REQUIRED TO DOUBLE THE BIRTH WEIGHT	PERCENTAGE COMPOSITION OF MILK (PARTIAL)			
		Protein	Ash	Calcium	Phosphorus
Human	180	1.6	0.2	0.02	0.02
Horse	60	2.0	0.4	0.09	0.06
Cow	47	3.5	0.7	0.12	0.09
Goat	22	3.7	0.78	0.14	0.18
Sheep	15	4.9	0.84	0.18	0.11
Swine	14	5.2	0.80	0.18	0.14
Dog	9	7.4	1.33	0.32	0.22
Rabbit	6	14.4	2.50	0.65	0.43

It is, however, not without possible significance that the phosphorus of human milk is mainly in organic forms (Söldner) and that, notwithstanding its much lower content of total phosphorus, human milk contains as high a percentage of lecithin as does cow's milk (Stoklasa). An infant fed on diluted cow's milk must therefore receive less lecithin than the breast-fed infant while it may receive more total phosphorus.

In general the more recent investigations favor the view that the body can use inorganic phosphates to meet all its phosphorus requirements.

Hart, McCollum, and Fuller showed in 1909 that with young pigs on a ration too poor in phosphorus to support normal growth the deficit could be made good by feeding phosphates as well as by feeding foods containing organic phosphorus compounds.

The following year (1910) McCollum reported that, other things being satisfactory, all the phosphorus requirements of an animal can be met by feeding inorganic phosphates. In one of these experiments McCollum kept a rat for 104 days on diets of purified food materials in which phosphorus was given only as phosphate. It maintained good condition but suffered some loss of weight as it would not eat enough of the artificial food to meet the energy requirement. In another case in which an amino acid mixture from the hydrolysis of beef muscle was added to the diet the food was eaten more readily and one rat increased in weight from 153 to 176 grams while receiving only inorganic phosphorus.

As young rats eat unpalatable food more readily than do adults, McCollum fed the ration containing phosphate as sole source of phosphorus to young growing rats, one of which ate the ration for 127 days, during which time he doubled in weight. At the end of this experiment the rat was killed and analyzed and found to be of normal composition. There was therefore no reason to doubt that the rat synthesized the nucleoproteins and phosphatids of his growing tissues from the inorganic phosphorus of his food.

Subsequent experiments by McCollum and Davis, as well as those of Osborne and Mendel described in connection with the discussion of proteins (Chapter III), afford many instances of long-continued growth of rats on rations made up of " isolated " foodstuffs in which all or nearly all of the phosphorus was in the form of simple phosphates.

In order to determine whether the synthesis of lecithin in the animal body can be demonstrated experimentally, McCollum, Halpin, and Drescher (1912) fed 3 hens for 10 weeks a ration consisting of 30 per cent skim milk powder and 70 per cent polished rice, both of which were freed from phosphatids. This diet it will be noted contained phosphoprotein as well as phosphate, but very little fat, and it was believed no phosphatid. The hens produced eggs in normal number and of normal composition. The phosphatid in the eggs produced was 27.65 grams per hen, and this was believed to have been synthesized rather than to have come from material previously stored.

Fingerling (1912) kept ducks for 8 months on a diet of potatoes, blood albumin, starch, and lime salts. The ducks laid normally and the phosphatid content of the eggs produced was determined. Since the phosphatid content of the food must have been small and the feces always contained some lecithin-like substances, and since the ducks did not lose weight, Fingerling concludes that the organic phosphorus compounds in the eggs were synthesized from inorganic phosphorus obtained in the food.

Later he fed the same ducks on food richer in organic phosphorus; and as they produced about the same number of eggs of similar phosphatid content he concluded that the egg-phosphatids were synthesized as readily from inorganic as from organic phosphorus compounds.

The evidence seems sufficient to warrant the statement that animal organisms are able to synthesize nucleoproteins, phosphoproteins, and phosphatids from inorganic phosphate. It may, however, still be questioned whether the nutritive conditions are as favorable when the body is forced to do this as when a part at least of the phosphorus requirement is met by feeding phosphoproteins and phosphatids.

The above-mentioned experiments of Rohmann and his pupils on dogs and of Ehrstrom and Gumpert on men seemed to demonstrate that the phosphoproteins have a higher food value than a corresponding mixture of simple proteins and simple phosphates; and the recent feeding experiments, while showing the efficiency of phosphates in meeting the phosphorus requirement, do not show conclusively that the phosphates are of fully equal value with the organic phosphorus compounds. Feeding experiments of long duration are well fitted to give convincing evidence on the former point, but are not so well suited for the purposes of exact quantitative comparisons because the very fact of their long duration gives opportunity for other factors to enter, such as differences in vitality among the experimental animals. Masslow, as the result of recent investigation of phosphorus metabolism during growth, holds (1913) that for the best results a considerable part of the phosphorus should preferably be supplied in organic forms.

Some writers have argued that the presence in extracts of intestinal mucosa of enzymes capable of splitting off phosphoric acid from the organic phosphorus compounds of the food may be taken as evidence that phosphorus is absorbed as phosphoric acid or phosphate whatever the form in which it occurs in the food; but in view of the reversibility of enzyme action and the great extent to which it is influenced by conditions, it seems preferable to form our impressions regarding the equivalence or relative values of the different phosphorus compounds from observations or experiments upon animals rather than from tests for enzymes in tissue extracts.

Forbes holds that even though the phosphorus be absorbed as inorganic phosphate there is advantage in having it supplied largely in organic forms since "much larger amounts of phosphorus may be utilized in a normal manner if they are gradually liberated in the usual way by the digestive cleavage of the organic complexes with which they are combined." *

Forbes and Keith (1914) after reviewing most thoroughly the whole literature of phosphorus compounds in animal metabolism, draw, among others, the following conclusion:

"That organic phosphorus is absolutely essential to any animal has not been demonstrated. The proof that inorganic phosphorus can serve all of the purposes for which any animal needs phosphorus is incomplete.† There is much evidence to imply that, with some species at least, some organic phosphorus compounds are more useful than is inorganic phosphorus in the sense of being more readily and economically utilized, and of maintaining a higher state of vitality as revealed by tissue enzyme estimations, the difference probably depending, in part at least, on the fact of the partial absorption and utilization of organic phosphorus compounds as such, without complete digestive cleavage" (Ohio Agricultural Experiment Station, Technical Bulletin No. 5, pages 364–365).

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* Ohio Agricultural Experiment Station, Technical Bulletin No. 5, page 357.

† (Some of the experiments of Osborne and Mendel and of McCollum and Davis have appeared since the above was written by Forbes and Keith. H. C. S.)

On the other hand Marshall * considers the evidence fully sufficient to warrant the conclusion that organic phosphorus compounds are of no more value as food than are the inorganic phosphates.

In the present state of our knowledge there is at least no quantitative measure of differences in nutritive value as between different forms of phosphorus. If differences in nutritive value between the different groups of phosphorus compounds exist, they are doubtless in favor of the phosphoproteins and phosphatids and are more significant for the growing than for the full-grown organism. For the reasons explained in Chapters VIII, XIII, and XIV the diet of growing children should always contain a liberal allowance of milk. The milk will provide, in addition to the best form of protein, a high proportion of phosphoprotein and also significant quantities of phosphatids. Hence it seems justifiable to assume that, if the food is properly selected, one may compute its total phosphorus content and compare it with the total phosphorus requirement of the body without separate computation of the different forms of phosphorus.

Estimation of the Phosphorus Requirement

Since phosphorus compounds are essential to all the tissues of the body, the growth of new tissue requires a storage of phosphorus along with that of protein, but aside from this it is evident that the phosphorus metabolism presents a separate problem from the metabolism of protein.

The phosphorus of the tissues exists largely in the form of nucleoproteins — the characteristic substances of cell nuclei — and, as these are important in metabolism, there was a tendency for a number of years to regard the phosphorus elimination as largely a measure of the metabolism of nucleoproteins somewhat as the nitrogen is taken as a measure of the

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* *Journal of the American Medical Association*, Vol. 64, page 573 (1915).

metabolism of proteins in general. It is probable, however, that such a view of the phosphorus metabolism is of only very limited application, because of the influence of other factors. Voit showed that the material metabolized in fasting comes largely from the bones. Undoubtedly the bones take part in the daily metabolism, and while they may undergo a less active exchange of material than the soft tissues, they possess such a large proportion of the phosphorus in the body that they probably contribute a considerable part of what is metabolized from day to day. Moreover, recent investigations upon the function of the soluble phosphates of the blood in maintaining neutrality in the body indicate that the neutralization of acid by conversion of di- into mono-phosphates may be followed by an increased excretion of the acid phosphate in the urine. Finally, it is evident that the amount of phosphorus metabolized is very directly influenced by the amount taken in the food.

The phosphorus which has been metabolized is excreted from the body almost entirely in the form of inorganic phosphates, the organic phosphorus of the urine constituting as a rule only 1 to 3 per cent of the total.* Carnivorous animals excrete phosphates mainly through the kidneys, but in the herbivora the excretion occurs almost entirely through the intestinal wall, whether the phosphate be taken by the mouth, or injected subcutaneously, or be formed by metabolism of organic phosphorus compounds in the body. In man, the elimination of metabolized phosphorus is partly through the kidneys and partly through the intestinal wall, the relative quantities in urine and feces varying within rather wide limits. As a rule, foods rich in calcium, or which yield an alkaline ash, tend to increase the proportion of phosphorus excreted by way of the intestine.

Attempts have sometimes been made to estimate the phosphorus requirement from the amount excreted in the urine.

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* Some investigators have doubted the occurrence of organic phosphorus in urine while others have estimated it as high as 6 per cent of the total urinary phosphorus.

The results thus obtained are always too low (usually very much so), and are largely responsible for the fact that the amount of phosphorus required for the normal nutrition of man is seriously underestimated in many of the standard textbooks.

Since the excretion of metabolized phosphorus through the intestine is in man too large to be neglected and too variable to be allowed for by calculation, we can expect reliable data on phosphorus requirements from those experiments only in which the amounts of phosphorus are actually determined in food, in feces, and in urine. In such experiments it is found (as in the case of nitrogen) that the output obtained upon the experimental days is influenced not only by the food taken at the time, but also by the rate of metabolism to which the body had been accustomed on the preceding days. This is shown by the following results obtained in a 12-day series of experiments upon a healthy man:

PHOSPHORUS METABOLISM WITH DIFFERENT AMOUNTS OF PHOSPHORUS IN THE FOOD

EXPERIMENTAL PERIOD		PHOSPHORUS PER DAY				
No.	DURATION	IN FOOD Grams	IN FECES Grams	IN URINE Grams	OUTPUT Grams	BALANCE Grams
I	3 days	0.40	0.45	0.70	1.15	− 0.75
II	6 days	0.77	0.19	0.72	0.91	− 0.14
III	3 days	1.51	0.50	0.99	1.49	+ 0.02

Here the output of phosphorus was greater in the first period with 0.40 gram in the food than in the second when the food furnished 0.77 gram, probably because the first period followed and was influenced by a preceding diet fairly rich in phosphorus, whereas the output in Period II was influenced by the low-phosphorus diet of Period I. For the same reason Period II offered favorable conditions for the establishment of equilibrium on a minimum diet, and the results show that in this case the subject was unable to reach equilibrium on 0.77 gram per day, the output averaging 0.91 gram. When the intake was increased to 1.51 grams, the output rose rapidly and averaged 1.49 grams. In this case the amount which would have been just sufficient for equilibrium evidently lay between 0.91 and 1.49 grams per day. By means of well-planned experiments or series of experiments it is possible to fix for a given individual much narrower limits within which the exact amount required for equilibrium must lie, and when it is known that the intake approximates this required amount, it is justifiable to regard the output as an indication of the normal nutritive requirement.

Study of the data of 93 such phosphorus balance experiments upon 27 subjects, 21 men and 6 women, has shown a range of 0.52 to 1.75 grams with an average of 0.96 gram phosphorus (2.20 grams P_2O_5) per 70 kilograms of body weight per day. This corresponds with the average requirement of 50 grams protein per day per man of 70 kilograms as estimated on page 220. Allowing 50 per cent above the bare minimum would give a phosphorus "standard" of 1.44 grams (3.30 grams P_2O_5) corresponding to a protein "standard" of 75 grams.

Phosphorus in Food Materials and Typical Dietaries

A comparison of the amounts of phosphorus contained in the food of typical American families with the amounts metabolized in the experiments above mentioned indicates that a freely chosen diet does not always furnish an abundance of phosphorus compounds. In 150 American dietaries of families or larger groups believed to be fairly representative, the estimated amount of phosphorus furnished per man per day was below 0.96 gram in 7 cases, while in no case was there less than 50 grams of protein per man per day. If we allow a margin of 50 per cent for safety in both protein and phosphorus, we find 8 per cent of the dietaries below the protein standard of 75 grams and 41 per

APPROXIMATE AMOUNTS OF PHOSPHORUS IN FOOD MATERIALS

FOOD	PHOSPHORUS PER 100 GRAMS EDIBLE SUBSTANCE	PHOSPHORUS PER 100 GRAMS PROTEIN	PHOSPHORUS PER 3000 CALORIES
Beef, all lean	0.218	0.96	5.2
Eggs	.180	1.35	3.66
Egg yolk	.524	2.73	3.54
Milk	.093	2.82	4.02
Cheese	.683	2.58	4.68
Wheat, entire grain	.423	3.25	3.54
White flour	.092	.81	.78
Rice, polished	.096	1.19	.81
Oatmeal	.392	2.36	2.97
Beans, dried	.471	2.20	4.11
Beets	.039	2.42	2.52
Carrots	.046	4.17	3.03
Potatoes	.058	2.60	2.07
Turnips	.046	3.55	3.51
Apples	.012	3.15	0.60
Bananas	.031	2.35	0.93
Oranges	.021	2.58	1.20
Prunes, dried	.105	5.00	1.05
Almonds	.465	2.25	2.16
Peanuts	.399	1.55	2.19
Walnuts	.357	1.96	1.53

cent below the phosphorus standard of 1.44 grams. These results indicate plainly that present food habits are more likely to lead to a deficiency of phosphorus compounds than to a deficiency of protein in the diet, and it is not improbable that many cases of malnutrition are really due to an inadequate supply of phosphorus compounds.

That the cases of low phosphorus dietaries are not to be ascribed simply to inadequacy of the total food supply of these families was shown by computing the amounts of phosphorus which would have been furnished in each case had the total amount of food been so increased or decreased as to furnish just 3000 Calories per man per day. On this basis only one of the 150 dietaries shows less than 0.96 gram, but 49 of them or 33 per cent show less than 1.44 grams of phosphorus, as against only 2 per cent with less than 75 grams of protein, per 3000 Calories.

The table on the preceding page compares some staple foods as sources of phosphorus.

It will be seen that, whether compared on the basis of weight, or of protein content or energy value, the different staple foods vary greatly in phosphorus content. In the planning of dietaries this fact should be kept in mind and care taken that foods fairly rich in phosphorus be adequately represented in each day's food.

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CHAPTER X

INORGANIC FOODSTUFFS AND THE MINERAL METABOLISM (Continued)

Metabolism of Sodium, Potassium, Calcium, Magnesium

THE distribution of sodium and potassium in the body and some of their mutual relations in metabolism have been referred to in the section on the chlorides. The distribution and functions of calcium have been studied in greater detail than those of magnesium. It is estimated that about 85 per cent of the mineral matter of bone, or at least three fourths of the entire ash of the body, consists of calcium phosphate. Probably over 99 per cent of the calcium in the body belongs to the bones, the remainder occurring as an essential constituent of the soft tissues and body fluids. Of the magnesium in the body about 71 per cent is contained in the bones (Lusk). The muscles contain considerably more magnesium than calcium; the blood contains more calcium than magnesium.

That calcium salts are necessary to the coagulation of the blood has long been known and frequently cited as an example of the great importance of calcium salts to the animal economy. Equally striking is the function of these salts in regulating the action of heart muscle.

It is well known that heart muscle may be kept beating normally for hours after removal from the body when supplied, under proper conditions, with an artificial circulation of blood or lymph or a water solution of blood ash. Howell, Loeb, and others have studied the parts played by the several ash constituents. The sodium salts take the chief part in the maintenance of normal osmotic pressure and have also a specific influence. Contractility and irritability disappear if they are absent, but when present alone they produce relaxation of the muscle tissue. Calcium salts also, although occurring in blood in very much smaller quantity, are absolutely necessary to the normal action of the heart muscle; while if present in quantities above normal, they cause a condition of tonic contraction ("calcium rigor"). There is a balance which must be maintained between calcium on the one hand and sodium (and potassium) on the other. Thus it is found that the alternate contractions and relaxations which constitute the normal beating of the heart are dependent in part upon the presence of a sufficient but not excessive concentration of calcium salts, and in part upon the quantitative relationship of calcium to sodium and potassium, in the fluid which bathes the heart muscle. Other active tissues of the body doubtless have analogous requirements as to inorganic salts.

Regarding the adequacy of the ordinary intake to meet the specific requirements for sodium, potassium, calcium, and magnesium, it would seem that only in the case of calcium is it ordinarily necessary to take thought in the selection of food materials or the arrangement of dietaries. The amount of sodium chloride usually added to food is much more than sufficient to meet the sodium requirement of the body, even if the natural sodium content of the food be entirely disregarded. Potassium and magnesium are relatively abundant in meat (muscle) and also in most plant tissues, so that an ordinary mixed diet, unless it consist too largely of highly refined food materials, will usually furnish a safe surplus of these elements. Dietaries entirely adequate in energy value and protein content may, however, contain too little calcium. Calcium requirement is therefore a question of much practical importance in human nutrition, and requires quantitative study.

The Calcium Requirement

Calcium constitutes a larger proportion of the body weight (about 2 per cent) than does any other of the "inorganic" elements. It is very unevenly distributed in the body, over 99 per cent of the total amount being in the bones. It is also very irregularly distributed among the staple articles of food, many of which are extremely poor in calcium, while milk contains it in abundance. The "ordinary mixed diet" of Americans and Europeans, at least among dwellers in cities and towns, is probably more often deficient in calcium than in any other chemical element.

In studying the effects of insufficient calcium, Voit kept a pigeon for a year on calcium-poor food without observing any effects attributable to the diet until the bird was killed and dissected, when it appeared that, although the bones concerned in locomotion were still sound, there was a marked wasting of calcium salts from other bones such as the skull and sternum, which in places were even perforated. Thus in adults there may be a continued loss of calcium without the appearance of any distinct symptoms because the losses from the blood and soft tissues may be replaced by calcium withdrawn from the bones. The injurious effect of an insufficient intake of calcium is of course more noticeable with growing than with full-grown animals. Abnormal weakness and flexibility of the bones (resembling the condition of rickets in children) has been produced experimentally by feeding puppies with lean and fat meat only, while others of the same litter, receiving the same food, but with the addition of bones to gnaw, developed normally. In this connection it should be remembered that no animal is literally carnivorous in nature, that is, none lives on flesh alone; the animals called carnivora always eat more or less of the bones of their prey.

According to Herter* many cases of arrested development in infancy may be due to an insufficient assimilation of calcium from the food. Such a deficiency in the amount assimilated may be due to defective digestion or to a diet inadequate in calcium content.

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* *On Infantilism from Chronic Intestinal Infection*, New York, 1908.

Many medical writers have attributed different diseases to inadequate calcium supply or disturbance of calcium metabolism. Conclusive proof or disproof of such theories would however require more detailed and exact quantitative studies of the intake and output of calcium in health, and the amounts required in normal nutrition at different ages and under different conditions, than have yet been made.

The fact that normal urine has a low calcium content while the feces usually contain much the greater part of the calcium which has been taken in the food has often been interpreted as meaning that the absorption of food calcium is poor or that the calcium requirement of the body is low. It is now known, however, from experimental evidence, that most of the calcium which has been absorbed and carried through the metabolic processes is normally excreted through the intestinal wall and thus leaves the body in the feces instead of the urine. When the diet is very poor in calcium and the output of this element materially exceeds the intake, the feces often contain a larger amount of calcium than was present in the food.

Observations upon Breithaupt and Cetti showed a considerable elimination of calcium in the feces during fasting. On the other hand, Benedict reports the result of a 31-day fast during which no feces were passed, but considerable quantities of calcium continued to be lost through the urine throughout the entire period.

On account of the fluctuating distribution of the calcium between urine and feces, conclusions regarding the calcium requirement can properly be drawn only from those experiments in which the amounts of this element in the food, in the feces, and in the urine have been directly determined. A compilation of such experiments has been made, and the reported results calculated to a uniform basis of 70 kilograms of body weight. On this basis, 63 experiments on 10 subjects (6 men and 4 women) show calcium outputs ranging from 0.27 to 0.78 gram and averaging 0.45 gram of calcium "per man per day." This includes the experiments which appear most reliable as indicating the actual (minimum) requirement in that the food did not furnish an excess of calcium over the needs of the subject, and the calcium balance showed a reasonable approach toward equilibrium. It will be noted that this average of 0.45 gram calcium (equivalent to 0.63 gram CaO) represents the expenditure under conditions of closely restricted calcium intake. It corresponds to the average of 49.2 grams of protein per man per day reached on page 220, and approximates the minimum of actual need rather than a normal allowance. The margin for safety should probably be larger for calcium than for protein because of the likelihood of relatively greater losses in cooking and in digestion, while there is much less danger of any injurious result from surplus calcium than from surplus protein. Nelson and Williams have recently found the calcium output of four healthy men on normal unrestricted diet to range from 0.68 to 1.02 grams of calcium (0.95 to 1.43 grams of CaO) per day. Here as in the case of protein the rate of metabolism to be expected in a normal man on unrestricted diet and well fed, according to American standards, runs from 50 to 100 per cent above the amount which would probably suffice to meet the actual requirement.

The calcium requirements of women are greatly increased by maternity. The need of an abundance of calcium for the rapidly growing skeleton of an infant is obvious. Before birth, and normally for several months after, this demand of the child is satisfied through the mother, whose calcium requirement is thus greatly increased. The weakening of the bones and teeth which is said to be a common accompaniment of pregnancy and lactation is held by Bunge to be largely due to a withdrawal of calcium from these structures to meet the nutritive requirements of the embryo or the nursling.

Lusk also emphasizes the importance of a diet rich in calcium for pregnant women, especially during the last ten weeks of pregnancy, when the fetus is storing calcium at a rapid rate. He cites * the data of Hoffström,† who computed in considerable detail the demands of the fetus upon the mother for nitrogen, phosphorus, calcium, and magnesium at different stages of intrauterine life.

Strong confirmation of this has recently been obtained from investigation of farm animals. The experiments of Steenbock and Hart show that the production of milk in cows and goats causes a heavy drain upon the calcium of the skeleton unless the amount of calcium contained in the food be very abundant. They also point out that the mammary glands likewise make large demands upon the phosphorus supply and suggest that if the food be not rich in phosphorus the destruction of bone tissue to furnish phosphorus for milk production may result in still further loss of calcium from the body.

Forbes and Beegle in studying the mineral metabolism of the milch cow found a heavy loss of body calcium, notwithstanding the fact that the food was believed to supply liberal amounts of all essential elements and was eaten in sufficient quantity to induce storage of nitrogen. That calcium may be lost from the body while nitrogen is being stored has also been emphasized by several other investigators (Steenbock and Hart, Weiser, and others). According to Forbes it may be necessary to continue high calcium feeding for some time after the cessation of lactation, in order to replace the calcium which the maternal organism has lost.

In children after weaning and throughout early childhood there are apt to be frequent disturbances of the absorption and metab-

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* Lusk. *Science of Nutrition*, 3d edition, pages 389–390.

† Hoffström. *Skandinavisches Archiv für Physiologie*, Vol. 23, page 326 (1910).

olism of calcium, in some cases due to distinct disorders of digestion, in other cases to more obscure irregularities in nutrition. In order that these fluctuations shall not interfere with the steady growth of the child, it is obvious that the food must furnish a fairly liberal surplus of calcium. Even under the most favorable conditions, a rapidly growing child will presumably need more bone-making material in proportion to its total food than do adults, who alone have served as subjects for the metabolism experiments upon which our present estimate of calcium requirement is based. Camerer, in summarizing a long series of investigations upon the food requirements of children at different ages, concluded that the amount of calcium received by the average nursling is just about sufficient to maintain a normal rate of growth, leaving little if any " margin of safety " ; and Bunge, from a comparison of the calcium contents of different staple foods, points out that calcium more than any other inorganic element is likely to be deficient as the result of the change of diet from mother's milk to other forms of food.

Herter * estimates that in order to support normal growth of the skeleton there must be an average storage of about 37 grams of calcium (51.6 grams of calcium oxide) annually throughout the period from the third to the sixteenth year. This means an average daily storage of somewhat more than 0.10 gram of calcium during this thirteen-year period. In order to accomplish such a storage it is plain that the daily food of the child must contain a surplus of more than 0.10 gram of calcium per day beyond the amount required for maintenance, which latter amount should provide for the frequent failures of complete utilization which have already been mentioned.

Herbst † studied the calcium metabolism of 6 boys between the ages of 6 and 14 years and found that they were storing from 0.010 to 0.016 gram of calcium per kilogram per day, or 0.21

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* *Infantilism.*

† *Jahrb. Kinderheilkunde,* Vol. 76. *Ergänzungsheft,* pages 40–130.

to 0.39 gram per capita per day. If normal growth of boys of these ages involves such a large storage of calcium, it is plain that the food of such boys must be rich in calcium if they are to develop advantageously. These boys consumed about 3 to 4 times as much calcium in proportion to their weight as is required for the maintenance of men.

From such considerations as these it is evident that one should be very liberal in calculating the amount of calcium to be supplied to growing children.

If 0.45 gram is the minimum on which an average man can maintain equilibrium, it would seem that the food of a family should furnish at least 0.67 gram * of calcium or 0.9 to 1.0 gram of calcium oxide per man per day. This is less than is advocated by such recent writers as Albu and Neuberg, Gautier, Obendoerffer, and Emmerich and Loew, or reported by Nelson and Williams; yet about 50 per cent of the American dietaries which have so far been studied with respect to their ash constituents show less than 0.67 gram of calcium per man per day, and about 15 per cent of them show less than 0.45 gram calcium (0.63 gram CaO) per man per day. In some cases the deficiency in calcium is incidental to a general deficiency in the amount of food; but if the food consumed in each dietary had been increased or decreased to just 3000 Calories there would have been less than 0.67 gram of calcium in 46 per cent, and less than 0.45 gram in 8 per cent of the cases. Since inorganic forms of calcium are utilized in nutrition, the lime of the drinking water may be added to that of the food in calculating the amount consumed, and to this extent the actual nutritive supply may be greater than the dietary studies show, but unless a very "hard" water be used for drinking, it is unlikely that the lime from this source will cover more than a small part of the calcium requirement. It is probable too that losses of food cal-

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* This amounts to setting a tentative "standard" 50 per cent higher than the average minimum, as in the cases of protein and of phosphorus.

cium in cooking may fully offset the calcium obtained from the drinking water. Apparently the American dietary is more often deficient in calcium than in any other element; certainly more attention should be paid to the choice of such foods as will increase the calcium content of the dietary. The use of more milk and vegetables with less meat and sugar will accomplish this and usually improve the diet in other directions as well.

Calcium Content of Typical Foods

The table on the following page shows the comparative richness in calcium of a number of staple articles of food.

It will be seen that there are enormous differences in the calcium content of different foods, whether expressed in percentage of the food material or in relation to its protein content or energy value. Meat is exceedingly poor in calcium and is therefore, notwithstanding its high protein content, a very one-sided and inadequate source of " building material." Milk is so rich in calcium that one need take only 400 Calories of milk to obtain the entire day's supply of this element, while to get the same amount of calcium from round steak and white bread it would be necessary to take 10,000 Calories. Polished rice and new process corn meal are even poorer in calcium than white flour. The difference in calcium content between the whole grains and the " fine " mill products, while not so great as in the case of iron or phosphorus, is still considerable. In general the milling removes more than half of the calcium. The fruits and vegetables in general are fairly rich in calcium, while some of the green vegetables are strikingly so; but in most cases the intake of calcium depends mainly upon the extent to which milk (and its products other than butter) enters into the dietary. A quart of milk contains rather more calcium than a quart of clear saturated lime water. By far the most practical means of insuring an abundance of calcium in the dietary is to use milk freely as a food.

APPROXIMATE AMOUNTS OF CALCIUM IN FOOD MATERIAL

Food	Calcium per 100 Grams Edible Substance	Calcium per 100 Grams Protein	Calcium per 3000 Calories
	grams	grams	grams
Beef, all lean	0.007	0.03	0.18
Eggs	0.067	0.5	1.35
Egg yolk	0.137	0.9	1.1
Milk	0.120	3.7	5.2
Cheese	0.931	3.5	6.4
Wheat, entire grain	0.045	0.33	0.40
White flour	0.020	0.18	0.18
Rice, polished	0.009	0.06	0.04
Oatmeal	0.069	0.4	0.5
Beans, dried	0.160	0.7	1.4
Beets	0.029	1.9	1.9
Cabbage	0.045	2.8	4.3
Carrots	0.056	5.1	3.7
Potatoes	0.014	0.6	0.5
Turnips	0.064	5.0	4.8
Apples	0.007	1.9	0.36
Bananas	0.009	0.7	0.27
Oranges	0.045	5.7	2.6
Prunes, dried	0.054	2.6	0.5
Almonds	0.239	1.2	1.1
Peanuts	0.071	0.3	0.4
Walnuts	0.089	0.5	0.4

Relations of the Inorganic Elements to Each Other

It is evident from what has already been seen that the custom which has been more or less prevalent of referring to the ash or mineral matter of a food as if it were *a substance* is wholly illogical and incorrect. Food ash is always a mixture of the compounds of several different elements, and each element has its own functions and significance in nutrition. Even elements so closely related chemically as are sodium and potassium, or calcium and magnesium, are not only not interchangeable, but are, in some of their functions, directly antagonistic in their action in the body. Bunge's experiment showing the effect of potassium upon sodium excretion has already been noted. Meltzer and his associates have shown that the injection of magnesium salts has a marked general inhibitory effect, and that this can be quickly overcome by the subsequent injection of calcium salt. Summarizing the results of extended series of investigations by himself and others, Meltzer stated, in the *Transactions of the Association of the American Physicians* for 1908:

"Calcium is capable of correcting the disturbances of the inorganic equilibrium in the animal body, whatever the directions of the deviations from the normal may be. Any abnormal effect which sodium, potassium, or magnesium may produce, whether the abnormality be in the direction of increased irritability or of decreased irritability, calcium is capable of reëstablishing the normal equilibrium."

More recently Hart and Steenbock have found that the addition of magnesium salts to an otherwise well-balanced ration tends to cause a loss of calcium from the body. Several other observers have reported similar unfavorable effects of magnesium upon the metabolism of calcium, and some are inclined to regard this as a matter of much importance to the well-being of the body. On the other hand, calcium seems to exert a favorable influence upon the economy of iron in metabolism, inasmuch as it appears to be possible to maintain equilibrium upon a smaller amount of iron when the food contains an abundance of calcium.

It would thus appear that an adequate study of the subject should take account of the relative, as well as the absolute, amounts of the different inorganic elements of the food. Tables showing these elements for the different articles of food are included in the Appendix at the back of this book. Not only do the different food materials differ greatly in the absolute and relative abundance of the different elements, but the same is also true of the total food intake of different groups of people. Studies of 150 freely chosen American dietaries each covering the food of a group of people for a week or more show the following range and average intake, per man per day and per 3000 Calories.

INORGANIC ELEMENTS IN 150 AMERICAN DIETARIES

ELEMENTS	PER MAN PER DAY			PER 3000 CALORIES		
	Min.	Max.	Average	Min.	Max.	Average
Calcium	0.24	1.87	0.73	0.35	1.47	0.73
Magnesium	0.14	0.67	0.34	0.17	0.53	0.34
Potassium	1.43	6.54	3.39	1.63	5.27	3.40
Sodium	0.19	4.61	1.94	0.22	4.83	1.95
Phosphorus	0.60	2.79	1.58	0.72	2.30	1.59
Chlorine	0.88	5.83	2.83	0.83	7.26	2.88
Sulphur	0.51	2.82	1.28	0.80	2.35	1.30
Iron	0.0080	0.0307	0.0173	0.0090	0.0234	0.0174

Since these dietary records did not show the quantities of salt used, the figures for sodium and chlorine in the table cover only the amounts in the food as purchased and are greatly below the actual intake of these elements. It will be seen that the intake of any given element may be widely different in the different dietaries, even though each represents the daily average for at least a week. To some extent this is due to the variable amounts of total food consumed, but even when the data are reduced to a uniform basis of 3000 Calories the differences between minimum and maximum are still quite wide.

Output of Inorganic Elements during Fasting

In view of the relationships discussed above it is of interest to examine the absolute and relative excretion of the different elements as recently reported by Benedict for a subject who fasted for thirty-one days.

URINARY EXCRETION OF DIFFERENT ELEMENTS DURING A 31-DAY FAST (BENEDICT)

DAY	NITROGEN gms.	CHLORINE gms.	PHOSPHORUS gms.	SULPHUR gms.	CALCIUM gms.	MAGNESIUM gms.	POTASSIUM gms.	SODIUM gms.
1	7.10	3.77	0.73	0.46	0.217	0.046	1.630	2.070
2	8.40	1.02	1.08	0.61	.243	.106	1.368	.926
3	11.34	0.79	1.10	0.68	.243	.106	1.368	.926
4	11.87	0.59	1.27	0.67	.243	.106	1.368	.926
5	10.41	0.41	1.15	0.65	.274	.098	1.445	.276
6	10.18	0.40	1.02	0.65	.274	.098	1.445	.276
7	9.79	0.55	0.80	0.62	.253	.070	.883	.154
8	10.27	0.32	0.80	0.64	.253	.070	.883	.154
9	10.74	0.31	0.93	0.66	.253	.070	.883	.154
10	10.05	0.28	0.86	0.61	.220	.072	1.006	.100
11	10.25	0.36	0.85	0.62	.220	.072	1.006	.100
12	10.13	0.31	0.74	0.62	216	.065	—	—
13	10.35	0.32	0.85	0.62	.216	.065	—	—
14	10.43	0.26	0.81	0.60	.236	.071	.814	.109
15	8.46	0.16	0.64	0.50	.236	.071	.814	.109
16	9.58	0.14	0.89	0.59	.214	.078	—	—
17	8.81	0.12	0.87	0.53	.214	.078	—	—
18	8.27	0.15	0.81	0.54	.251	.059	.676	.051
19	8.37	0.16	0.77	0.55	.251	.059	.676	.051
20	7.69	0.15	0.64	0.51	.237	.053	.644	.066
21	7.93	0.18	0.70	0.51	.237	.053	.644	.066
22	7.75	0.21	0.69	0.50	.179	.050	.643	.083
23	7.31	0.18	0.71	0.51	.179	.050	.643	.083
24	8.15	0.10	0.68	0.49	.167	.056	.787	.065
25	7.81	0.18	0.67	0.49	.167	.056	.787	.065
26	7.88	0.16	0.65	0.54	.153	.051	.656	.055
27	8.07	0.16	0.62	0.52	.153	.051	.656	.055
28	7.62	0.14	0.59	0.53	.131	.047	.585	.036
29	7.54	0.12	0.64	0.52	.131	.047	.585	.036
30	7.83	0.14	0.61	0.52	.138	.052	.606	.053
31	6.94	0.13	0.58	0.49	.138	.052	.606	.053

It will be noted that the nitrogen output and the output of chlorine run entirely different courses, especially in the early days of the fast. Each of the other elements seems to run its own course except that the sulphur tends to remain relatively constant like the nitrogen (both being derived from protein metabolism), and the output of sodium tends to run parallel with that of chlorine, since these two elements are excreted mainly in combination with each other as common salt.

The Maintenance of Neutrality in the Body

One of the interesting relationships among the ash constituents of foods is that between the acid-forming and the base-forming elements, since this has a direct bearing upon the important problem of the maintenance of neutrality in the body.

Although the reaction of normal human blood is alkaline to litmus, the actual excess of hydroxyl over hydrogen ions is found by modern methods to be so slight that blood as well as protoplasm is commonly spoken of as neutral. Thus Henderson writes: "Neutrality is a definite, fundamental, and important characteristic of the organism."

The normal processes of metabolism, however, involve a continual production of acid (chiefly carbonic, phosphoric, and sulphuric) which must be disposed of in order to maintain this neutrality.

The factors generally recognized as concerned in the maintenance of neutrality are: (1) carbonates, (2) phosphates, (3) ammonia, (4) proteins.

As preliminary to even a brief mention of the function of these different mechanisms for maintaining neutrality, it may be well to recur for a moment to the fundamental conceptions which have recently been so well summarized by Henderson as follows: *

"First, the product of the concentrations of hydrogen and hydroxyl ions (at constant temperature) is approximately constant.

$$(H^+) \cdot (OH^-) = c$$

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* *Science*, Vol. 46, page 78 (July 27, 1917).

Therefore the concentrations of these two ions always vary inversely

$$(H^+) = \frac{c}{(OH^-)}$$

"Secondly, if for convenience, just as the histologist uses microns instead of meters, we adopt as unit concentrations of hydrogen and hydroxyl ions a very small quantity, viz. the concentration of these ions in neutral solutions, the value of this constant becomes unity.*

$$(H^+) \cdot (OH^-) = 1,$$
$$(H^+) = \frac{1}{(OH^-)}$$

It may be noted that, using this unit of concentration, an ordinary decinormal solution of hydrochloric acid has a concentration of hydrogen ions of nearly 1,000,000; and a decinormal solution of sodium hydroxide, a corresponding concentration of hydroxyl ions.

"Thirdly, upon this basis the definitions of neutrality, acidity, and alkalinity are as follows:

For neutrality,

$$(H^+) = 1 = (OH^-)$$

For acidity,

$$(H^+) > 1 > (OH^-)$$

For alkalinity,

$$(H^+) < 1 < (OH^-)$$

"Finally, in any solution containing a weak acid and its salts with one or more bases, regardless of the other components of the solution, the concentration of hydrogen ions is approximately proportional to the ratio of free acid to combined acid.

$$(H^+) = k\frac{HA}{BA}$$

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* The more usual method of expressing hydrogen ion concentration has been referred to in an earlier chapter (page 77).

This relation, however, holds only when the ratio of acid to salt is neither very large nor very small.

"It is therefore evident that in the solution of any weak acid, when the quantities of free and combined acid are equal, the value of (H^+) is k; if the ratio of acid to salt be 10 : 1, (H^+) is 10 k, if the ratio be 1 : 10, (H^+) is 0.1 k."

In the case of carbonic acid and of acid phosphates the value of k is near enough to unity so that solutions containing acid carbonate or a mixture of primary and secondary phosphates must always remain nearly neutral.

Carbonic acid produced in metabolism is chiefly disposed of by elimination as carbon dioxide through the lungs. For description of the mechanism and regulation of carbon dioxide elimination the reader must be referred to discussions of the physiology of respiration. Its bearing upon the problem of neutrality is summarized by Henderson as follows:

"This substance is the chief excretory product of the organism. As such it must be eliminated promptly and completely. Moreover, in that it leaves the body not in aqueous solution and as an acid, but almost exclusively in the form of gaseous carbon dioxide, there is no possibility of any variation of the permanent effect produced upon the reaction of the body by the elimination of a definite amount of it. In the final regulation by excretion it is not, therefore, concerned. And yet it has, in the process of excretion, a very important rôle in regulating the reaction of the body. This depends upon the fact that carbonic acid is not only a waste product, but also a normal constituent of the blood, and, as such, a principal factor in the physicochemical regulation. Thus, if the ratio of carbonic acid to bicarbonates in a normal individual were 1 : 15, a large production of acid might cause a destruction of a third part of all the bicarbonates, producing in its place an equivalent amount of free carbonic acid. This, if nothing else occurred, would reduce the relative amount of bicarbonates from 15 to 10, and simultaneously increase the free carbonic acid from 1 to 6. The ratio would now be 6 : 10, and since the hydrogen ion concentration is proportional to this ratio, this ion would suffer a nearly tenfold increase of concentration. But at this point, or, more strictly speaking, continuously during the process, the excretory function intervenes. There is a tendency for the respiratory process to hold the tension of carbon dioxide in the blood nearly constant. This is the reason why carbonic acid has sometimes been thought the respiratory hormone. Assuming that the exact quantity of carbonic acid set free by the reaction of neutralization were thus eliminated, the ratio would be reduced to 1 : 10, and the hydrogen ion concentration would rise but one third above its original value. More recent investigations, however, have shown that a tendency to acidity is accomplished by a lowering of the tension of carbon dioxide. Let us suppose that in this case the tension was lowered one third. The free carbonic acid of the blood would then become 0.67 instead of 1.00, and the ratio of acid to salt 0.67 : 10, which is exactly equal to 1 : 15, the original ratio. Accordingly, the hydrogen ion concentration would be restored exactly to its original value, and the regulation by excretion would be quite perfect. Now there is abundant evidence to show that something very much like this is always occurring in the body, and, on the whole, I believe that the most delicate of all means to regulate the reaction of the body is to be found in this variation of the tension of carbonic acid during its excretion. Such considerations have strengthened the hypothesis that the hydrogen ion is the true respiratory hormone." (Henderson, *loc. cit.*)

Phosphates are regularly present in blood and urine in notable amounts. From what has already been seen regarding the reaction of the blood, it may be inferred that in it the primary and secondary phosphates are normally present in such proportions as to produce a practically neutral mixture. In urine, on the other hand, acid phosphate predominates, because the kidney usually removes from the blood a larger proportion of primary than of secondary phosphate. Thus by virtue of this ability of the kidney to secrete an acid urine from a neutral blood, the excess of phosphoric acid produced in metabolism is readily disposed of. The disposal of the sulphuric acid produced in the metabolism of protein is a more complicated problem. Sulphuric is so strong an acid that it would soon poison the body unless quickly neutralized.

When a fairly strong acid such as the sulphuric acid produced in the metabolism of protein enters a neutral or slightly alkaline solution of phosphates and carbonates such as the blood, it reacts with secondary phosphate to form primary phosphate and with bicarbonate to form carbonic acid. Since secondary phosphate (K_2HPO_4 or Na_2HPO_4) is but faintly basic, and primary phosphate (KH_2PO_4 or NaH_2PO_4) is but faintly acid, the ratio of these phosphates may be considerably changed (*i.e.* a considerable amount of strong acid may be received by the phosphate mixture) without appreciably diminishing the alkalinity of the solution. Thus the blood may neutralize a considerable amount of acid without appreciable change in its reaction, or as ordinarily expressed, without alteration of its own neutrality.*

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* This property is also referred to as the "buffer effect" of phosphate solutions and is of course connected with the capacity for secondary ionization, readily reversible according to the reaction of the medium:

$$\overset{\xleftarrow{\text{Acid}}}{H_3PO_4} \rightleftarrows H_2PO_4^- \rightleftarrows HPO_4^= \rightleftarrows \overset{\xrightarrow{\text{Alkaline}}}{PO_4^\equiv}$$

or

$$\begin{array}{ll} H_3PO_4 \rightleftarrows & H_2PO_4^- + H^+ \\ & \;\;\uparrow\downarrow \\ & HPO_4^= + H^+ \\ & \;\;\uparrow\downarrow \\ & PO_4^\equiv + H^+ \end{array}$$

For discussion of acid-base equilibria in phosphate solutions see the works of Henderson cited at the end of the chapter.

Ammonia, which is continually being formed in the body by deaminization of amino acids in the course of protein metabolism, constitutes another means of neutralization of acid. It will be remembered that, according as more or less acid is formed in, or introduced into, the body, a larger or smaller proportion of the nitrogen eliminated appears in the urine as ammonium salts.*

Proteins, such as those of blood serum, are amphoteric substances and can unite with acid by virtue of their amino, and perhaps other basic, groups. The constant presence of proteins in all parts of the body constitutes, therefore, a further mechanism for the immediate fixation of any strong acid produced. This, however, is only a temporary and partial solution of the problem, since the acid thus fixed would remain to be disposed of when the protein is hydrolyzed to amino acids.

The relations of these different factors in the maintenance of neutrality under normal conditions are summarized by Henderson as follows: †

"The hydrogen ion concentration of the body has been seen to depend on the ratio

$$\frac{H_2CO_3}{NaHCO_3}$$

Acid reacting with this system causes a diminution of the denominator and an increase in the numerator of the fraction, the value of the fraction increases, and with it the hydrogen ion concentration. Hereupon the lung reduces the value of the numerator by diminishing the concentration of carbon dioxide in blood and alveolar air, the value of the fraction is restored more or less exactly to its original value and with it the concentration of the hydrogen ion. But the denominator is still below normal. To offset this, there occurs, on the one hand, a production of ammonia which takes the place in the urine of alkali existing as salt in the blood. This alkali recombines with carbonic acid, forming bicarbonate, and thus increasing the denominator. On the other hand the kidney removes less alkali in combination with phosphates than exist in this state in the blood. This alkali, too, helps to regenerate sodium bicarbonate, and thus to increase the denominator. Both of these processes are so regulated that the denominator is restored to normal. The concentration of carbonic acid responds through the activity of the respiratory mechanism, and the organism returns to its normal state.

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* Two facts should, however, be kept in mind as possibly limiting the utility of this means of disposing of acid. In the first place, ammonium salts are generally regarded as somewhat toxic, their accumulation in the body being normally prevented by conversion into urea. Secondly, there is no good reason to suppose that the deaminization processes which form ammonia will always go on in the same cells and at the same time with the oxidation processes which produce sulphuric acid.

† *Loc. cit.*, page 81.

"These processes, of course, go on simultaneously and not in succession. They are, moreover, far less simple than such an analysis admits, for on the one hand the interaction of phosphates and proteins has not been fully described, and, on the other hand, many of these variations influence other conditions and processes in the organism."

The normal fluctuations of fixed acid production in healthy man on ordinary mixed diet are apparently taken care of in part by neutralization with ammonia and in part by the formation and excretion of acid phosphate. In an experiment upon man by Gettler and the writer it was found that, of the extra acid formed in metabolism as the result of replacing the potato of a mixed diet by rice, about 33 per cent was accounted for by the increased ammonia and about 40 per cent by the increased acidity of the urine, leaving a remainder which may have been eliminated, in part at least, through the skin, since no attempt was made to measure the amount or acidity of the perspiration, or may have been neutralized by sodium or potassium carbonate in the blood or other fixed alkali from the body. In this experiment the intake and output of phosphorus was approximately the same on both diets. The increased acidity of the urine, therefore, implied an increased ratio of primary to secondary phosphate in the urine but not necessarily any increase in the amount of fixed base leaving the body. In the neutralization of sulphuric acid by means of phosphate, each molecule of hydrogen sulphate (representing one atom of sulphur oxidized in protein metabolism) changes two molecules of secondary into primary phosphate. In order that the original condition of equilibrium may continue, the surplus acid phosphate thus formed must be excreted. Whether or not this results in an increased excretion of phosphates and therefore of sodium or potassium (or only, as in the experiment just cited, an altered ratio of primary and secondary phosphates in the urine), apparently depends not only upon the balance of acid-forming and base-forming elements in the food, but also upon the quantities of fixed bases and of phosphates which are being metabolized and of ammonia available from the protein metabolism. It would seem that in any case in which sulphuric acid produced in metabolism is neutralized by the sodium or potassium carbonate of the blood, the resulting sulphate must be eliminated with corresponding loss of sodium or potassium and decrease of the capacity of the blood for combining with carbon dioxide. This is an important feature of acidosis. It is diagnosed by determining the carbon-dioxide-holding capacity of a sample of blood serum and the result is expressed as the " alkali reserve " or " reserve alkalinity " of the blood.

Thus while the phosphates and carbonates of the blood and tissues serve for the immediate neutralization of acid without appreciable change in the normal reaction of the blood or tissue itself, yet when much strong acid such as the sulphuric acid from protein metabolism is neutralized in this way, there is apt to result an increased output of the base-forming elements, which if not made good by the intake must tend to diminish the " reserve alkalinity " or " alkali reserve " of the body.

That an excess of acid-forming elements in food, even if long continued, does not necessarily lead to any apparent injury is shown by experiments of McCollum, in which rats were maintained throughout a large part of their adult lives and produced healthy young on a diet of egg-yolk, in which there is a great predominance of acid-forming over base-forming elements. Yet in man an increase in the ammonia content and acidity of the urine is usually regarded (if pronounced and persistent) as indicating an unfavorable tendency. In this connection the decreased uric acid solvent power of the more acid urine is to be considered, especially in view of the present belief that the human organism does not destroy uric acid but must transport and excrete all that is produced in the body. Hindhede * found that the eating of vegetables, particularly potatoes, increases the capacity of the urine for dissolving uric acid. Furthermore, Hasselbalch † showed that the carbon dioxide tension of the alveolar (expired) air, which is indicative of the carbon-dioxide-carrying capacity and therefore of the reserve alkalinity of the blood, is influenced in a similar way by the food. On a diet rich in meat he found a tension of 37.8 mm.; on an ordinary mixed diet, 38.3 mm.; on a vegetarian diet, 43.3 mm.

In an extended series of experiments, Blatherwick ‡ likewise finds that foods which have a preponderance of base-forming elements lead to the formation of a urine which is less acid, both as regards hydrogen ion concentration and titration acidity, and which has an increased capacity for dissolving uric acid, while the ammonia content of the urine is diminished and the carbon dioxide tension of the alveolar air, indicative of reserve alkalinity, is increased. Conversely, foods with a predominance of acid-forming elements increase the urinary acidity and urinary ammonia, decrease the uric acid solvent

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* *Skandinavisches Archiv für Physiologie*, Vol. 26, pages 87, 384 (1912).

† *Biochemisches Zeitschrift*, Vol. 46, page 403 (1912).

‡ *Archives of Internal Medicine*, Vol. 14, pages 409–50 (1914).

power, and show, through lowered carbon dioxide tension of the alveolar air, a tendency toward depletion of the reserve alkalinity of the blood.

The benefit to health which so generally results from a free use of milk, vegetables, and fruits in the diet may be attributable in part to the fact that these foods yield alkaline residues when oxidized in the body; but this point should not be too greatly emphasized, for there are several other respects in which the eating of liberal amounts of milk, vegetables, and fruits is certainly beneficial, notably in supplying calcium, iron, and vitamines, and in improving the intestinal conditions.

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CHAPTER XI

IRON IN FOOD AND ITS FUNCTIONS IN NUTRITION

THE amount of iron contained in the body is small, but its functions are of the highest importance. As previously noted, the iron content of the adult man or woman is estimated at only 0.004 per cent, or 1 part in 25,000 parts of the body weight, or rather less than 3 grams (hardly one tenth of an ounce) in the entire body. Much the greater part of this iron exists as a constituent of the hemoglobin of red blood corpuscles and is constantly functioning in the general metabolism as the carrier of the oxygen upon which all of the oxidative (energy-yielding) processes of nutrition depend. There is no considerable reserve store of relatively inactive iron in the body corresponding to the store of calcium and phosphorus in the bones. Hence if the intake of iron fails to equal the output there must soon result a diminution of hemoglobin, which if continued must mean a greater or less degree of anemia. The investigation of iron metabolism has therefore been largely connected with the study of anemia and of hemoglobin formation.

Important changes of view in regard to the metabolism of iron have followed so closely and have depended so directly upon the progress of experimental methods that it seems desirable, in this case, to review in chronological order some of the more important steps in the development of our present knowledge.

Development of Modern Views

It has long been known that iron is essential to the nutrition of both plants and animals, and that small amounts of the oxide or phosphate of iron occur in the ash of all natural food materials. A few decades ago it was assumed that the iron exists in the food as oxide or phosphate, and that hemoglobin is formed in the body by the combination of protein with inorganic iron. This view was hardly consistent with the ideas of animal metabolism taught by Liebig and generally held at the time, but appeared to be supported by the successful use of inorganic iron in the treatment of anemia.

The results obtained in a number of investigations published between 1854 and 1884 threw doubt upon the utilization of inorganic iron for the production of hemoglobin, since they indicated that iron salts when injected act as poisons and are quickly eliminated from the blood, and when given by the mouth reappear almost quantitatively in the feces, little, if any, evidence of absorption being obtained except when the doses were so large or long continued as to cause irritation of the intestine.

In the attempt to harmonize this result with clinical experience it was suggested that the inorganic iron might act by absorbing the hydrogen sulphide of the intestine, thus protecting the food iron from waste.

The view that medicinal iron acts by stimulation of the absorbing membrane was also advocated at about this time. It was held that the amount of iron in the ordinary food is always sufficient for the needs of the body, but that sometimes the intestinal mucous membrane becomes so bloodless that it cannot properly perform its functions of absorption. Under such conditions inorganic iron was believed to stimulate and tone up the membrane so that in a short time the increased absorption of food iron makes good the deficiency in the blood.

A very suggestive discussion of the metabolism of iron, the effects of a lack of iron in the food, and the amounts of iron required for the maintenance of the body in health was published by Von Hösslin in 1882, and long before this some attention had been given to the iron content of food materials by Boussingault. Boussingault's figures, however, are not sufficiently accurate to be of value at the present time, and little attention was given to the subject discussed by Von Hösslin until it was reopened by Bunge about two years later.

Bunge, in 1884, doubting the ability of the animal body to form hemoglobin from inorganic iron, undertook the study of the iron compounds of food materials in order to find in what form iron is normally absorbed and from what sort of iron compounds the growing organism ordinarily forms its hemoglobin. Practically all of the iron of eggs was found to be in the yolk. Yolk of egg does not contain any hemoglobin, but it must contain substances from which hemoglobin can be formed, since the incubation of the egg results in the development of hemoglobin without the introduction of anything from without. Bunge found no inorganic iron in egg yolk, but isolated considerable amounts of the precursor of hemoglobin, which he called " hematogen," and which exhibited the properties of a phosphoprotein containing about 0.3 per cent of iron in such firm " organic " combination that it gives none of the ordinary reactions of iron salts. In milk, cereals, and legumes similar organic compounds of iron and only traces of inorganic iron were found. At this time Bunge distinctly stated that iron occurs in food solely in the form of complicated organic compounds which have been built up by the life processes of plants. In this form, said Bunge, is the iron absorbed and assimilated, and from these compounds hemoglobin is produced.

In 1890 and subsequently, the absorption and assimilation of iron was studied by several experimenters, usually with particular reference to the question whether inorganic or synthetic organic compounds of iron are absorbed and assimilated, and especially whether such preparations contribute directly to the formation of hemoglobin. This question is, of course, extremely important, not only in connection with the therapeutic use of medicinal iron, but also in its bearing upon the iron requirements in health; for if inorganic iron could be utilized in the body in exactly the same way as the complex organic iron compounds of the food, it would follow that the iron of drinking water could replace that of food, and the supplying of food iron would be a matter of indifference to a man whose drinking water supplied a few milligrams of iron per day. In opposition to this view, Bunge held that little if any inorganic iron is assimilated, and that any effect of medicinal iron should be attributed to its action in protecting the food iron from loss in digestion, principally by absorbing the sulphur liberated as sulphide through intestinal putrefaction.

Socin demonstrated the superiority of the iron of egg yolk over iron chloride by dividing a number of mice into groups, some of which were fed on a mixture of iron-free food and iron chloride, while others received the same iron-free food with the addition of egg yolk. None of the mice fed without organic iron lived for more than thirty-two days, while some of those receiving egg yolk lived as long as the experiments were continued (sixty to ninety-nine days), and gained in weight.

Gottlieb, recognizing the fact that iron might be absorbed and used by the body, yet finally excreted with the feces, determined the intestinal elimination of iron in dogs before and after subcutaneous and intravenous injections of known amounts of iron salts. From the results obtained it was estimated that practically all of the injected iron was eliminated by the intestines.

Voit studied the metabolism of iron in dogs by direct observations of absorption and elimination in isolated sections of the small intestine. Opening the peritoneal cavity, he separated the desired section, removed the contents, closed the ends, and left the sac thus formed in its normal position after having reunited the remainder of the intestine. Under these conditions the isolated section of intestine, while not coming in direct contact with anything taken by the mouth, would still receive its proportional share of anything eliminated from the body through the intestinal wall. By killing and examining animals which had been kept for some time after such an operation, Voit was able to compare the amount of iron eliminated through the intestinal wall with the amounts contained in food and feces, and thus to infer the extent to which the iron taken by the mouth was absorbed and returned to the intestine for elimination. In fasting, the daily elimination found for each square meter of intestinal surface was 6 milligrams in the feces and the same amount (per square meter of surface) in the isolated loop of intestine. On food poor in iron the feces contained in each of two cases 10 milligrams, the isolated loops 6 and 9 milligrams, of iron per square meter of intestinal surface; while on food rich in iron the corresponding figures for two experiments were 43 and 78 milligrams in the feces, and 8 and 6 milligrams in the isolated portion of the intestine. Hence it appears that the iron eliminated in the feces during fasting or on food poor in iron came from the body through the intestinal wall, while most of the extra iron given with the food in the last two experiments passed through the alimentary canal without being absorbed and metabolized.

Stockman, in a paper upon the metabolism of iron, published in 1893, while discussing mainly the therapeutics of chlorosis (a type of anemia occurring in girls and young women) undertook to solve the question of the absorption of inorganic iron. He reasoned as follows:

If inorganic iron preparations given hypodermically will cure chlorosis, there can in such cases be no possibility of the iron exerting its effect by the stimulation of the alimentary canal or by combining with hydrogen sulphide in the intestine.

If iron sulphide given by the mouth cures chlorosis, it must be through absorption of the iron, since ferrous sulphide has no stimulating effect and cannot take up more sulphur.

If bismuth, manganese, etc., take up hydrogen sulphide as readily as iron, but are inert in chlorosis, a further indirect evidence of absorption of iron is obtained.

Stockman made experiments and observations upon hospital patients (of which he cites nine cases) which appeared to substantiate each of the three propositions, and thus to establish the fact that inorganic iron preparations cure chlorosis through being absorbed and utilized in the formation of hemoglobin.

During the years 1894-1897 several investigators studied the absorption of different forms of iron by microchemical methods. Suitable stains having been found for the identification of iron in the microscopic sections of tissue, it was possible by examination of the intestinal wall and the various organs and tissues of the body to follow the absorption, storage, and elimination of the iron given medicinally or occurring in the food. Macallum investigated in this manner the behavior of inorganic salts of iron, iron albuminates, and the iron compound of the egg yolk, and found that iron taken in any of these forms may be absorbed from the small intestine.

Woltering compared microchemically and by quantitative determination the amounts of iron in the livers of mice, rabbits, and dogs, fed with and without sulphate of iron, and reported an increase in the iron content of the liver and in the hemoglobin and red corpuscles of the blood as the result of feeding the iron salt.

Gaule, using principally microchemical methods, found no reaction for iron in the chyle under normal conditions; but a distinct reaction appeared in the lymph nodes, and extended to the spleen soon after the feeding of iron salt to rabbits. This absorption of inorganic iron was followed by an increase in the number of red corpuscles and percentage of hemoglobin in the blood.

In the meantime, Kunkel and Egers studied especially the influence of iron salts upon the regeneration of blood after hemorrhage. Kunkel kept two dogs on a limited milk diet, but gave one of them, in addition to the milk, iron in the form of albuminate. Each of the animals was bled every seven days, about one third of the total blood being taken each time. The iron in the drawn blood was determined and ascertained to be greater than the amount supplied by the milk, but less than the total iron received by the dog which was fed with albuminate. The experiment was continued seven weeks, at the end of which time the blood and organs of the dog which had been kept on milk alone were poorer in iron than those of the dog which had received the iron albuminate. Only one animal was fed in each way, and no determinations of hemoglobin are recorded. According to Egers, the regeneration of blood after severe losses (one third of the estimated total) is very slow on food poor in iron, unless medicinal iron is also given, when the rate of regeneration becomes better, but not so good as on a diet supplying an abundance of food iron alone. Even when the diet was rich in food iron, however, Egers found that medicinal iron appeared to aid the regeneration of blood after hemorrhage.

These investigations having shown that inorganic iron is at least to some extent absorbed and carried to organs which take part in the production of hemoglobin, it became of especial importance to determine by long-continued feeding experiments whether the inorganic iron thus absorbed can take the place of food iron in the production of hemoglobin under normal conditions.

This question was studied by Häusermann in an extended series of experiments in Bunge's laboratory. The general plan of these experiments was to feed young animals from the end of the normal suckling period upon food poor in iron, usually milk and rice. One half of the animals, however, received ferric chloride in addition to this food. After the animals had been thus fed for from one to three months and had usually doubled in weight, they were killed, and the amount of hemoglobin in the entire body was estimated; also, in the case of small animals, the total amount of iron. Experiments were carried out in this way upon 24 rats, 17 rabbits, and 14 dogs. The results are summarized essentially as follows by Bunge: *

The rats all became highly anemic, for at the end of the experiment the percentage of hemoglobin was diminished to about half that of animals from the same litter which had received their normal food, namely, meat, flies, yolk of egg, fruit, and vegetables. The rats which had taken ferric chloride in addition to the milk and rice contained no more hemoglobin than those which had received milk and rice only. Moreover, the amount of iron was in each case the same. In one experiment alone, in which the addition of ferric chloride was continued for three months, was the iron found to be double as much in the animals which had received it as in those which had only milk and rice. But here again the proportion of hemoglobin remained the same in both instances. We thus see that some iron is absorbed if small doses of iron are persisted in for a long time, as well as if large amounts be suddenly administered. But this inorganic iron, when absorbed, is not utilized in the formation of hemoglobin to any appreciable extent, but remains unused in the tissues. Whether inorganic iron was absorbed in the experiments which lasted only from one to two months cannot be decided; it is possible that some of it was absorbed and was again eliminated in the same degree. Certainly no storing up nor increase of iron could be detected in the whole organism.

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* *Physiological and Pathological Chemistry,* Blakiston's edition, Philadelphia, 1902, page 379.

The experiments on rabbits gave less decisive results. The average proportion of hemoglobin in the animals that received inorganic iron was somewhat higher than that in the animals which were fed on milk and rice only. But when the great individual differences between various animals are taken into consideration, too much importance must not be ascribed to this slight divergence. At any rate, the amount of hemoglobin in the control animal, which received its normal diet — fresh green cabbage, bran, etc. — was nearly twice as high as in the animal which received the inorganic iron.

The experiments upon dogs were not attended with decisive results, as dogs are not suitable animals for these experiments, owing to the variation in individuals. Moreover, the growth of these animals after the period of lactation is at a much slower rate, and their appetite is so enormous that they might readily be able to assimilate sufficient iron for hemoglobin formation even from a material so poor in iron as milk. In fact, Häusermann found the largest proportion of hemoglobin in a dog which had been fed exclusively upon milk. The animals which received ferric chloride in addition to a milk diet certainly contained no more hemoglobin than animals from the same litter which were fed on meat and bones.

Abderhalden, following Häusermann, studied the subject even more exhaustively. In order to ascertain whether and to what extent sulphides normally exist in the alimentary canal, — a question of special importance in connection with one view of the mode of action of inorganic iron, — Abderhalden killed and examined rats, mice, cats, dogs, guinea pigs, and rabbits in the following way: Immediately upon killing the animal, the abdomen was opened and the intestinal tract from the esophagus to the rectum was ligated in sections. The contents of each section were then removed and tested qualitatively for sulphides. Hydrogen sulphide was obtained from the contents of the large intestine, but not from those of the small intestine nor of the stomach. Hence, if inorganic iron acts by improving the absorption of food iron, it must do so in some other way than by simply preventing its precipitation as sulphide, since this would not occur in the small intestine, where the principal absorption of iron takes place. The next step in the investigation was to study by microchemical methods the absorption of inorganic iron, its behavior in the body, and its elimination. Experiments were made upon 49 rats from 7 litters, 14 guinea pigs from 6 litters, 12 rabbits from 2 litters, 10 dogs from 3 litters, and 6 cats from 2 litters.

From all of these experiments, Abderhalden concluded that the complicated iron compounds of the normal food, the iron in the form of hemoglobin, and hematin, and the inorganic iron, were all absorbed in the same general way, stored in the same organs, and eliminated by the same paths.

In studying the utilization by the body of the different forms of iron, Abderhalden fed animals from the end of the suckling period, or, in the case of guinea pig, from birth, on food poor in iron, and divided each litter into two groups, one of which was given inorganic iron in addition. After a sufficient time the animals were killed, and the total hemoglobin in the body of each was estimated. Experiments of this kind were made upon 48 rats, 44 rabbits, 14 guinea pigs, 17 cats, and 11 dogs. The animals fed with food poor in iron plus an addition of inorganic iron were unable to produce as much hemoglobin as those receiving normal food.

In these experiments, Abderhalden had noticed some facts which indicated that the favorable influence of inorganic iron upon metabolism and blood formation was greater on a diet rich in food iron than when the amount of food iron was kept small. In order to test this, experiments were made with 66 rats, 10 rabbits, and 14 guinea pigs, in the manner already described, but with diets arranged to bring out this particular point. These experiments led to the conclusion that the greater the quantity of food iron present, the greater the influence of the inorganic iron upon the hemoglobin formation.

Abderhalden's experiments also showed that the production of hemoglobin was not stimulated indefinitely by inorganic iron, but only for a short time, and he concluded that, while inorganic iron may be absorbed and may favorably influence blood formation, it is not used as material for the production of hemoglobin. It has also been found clinically that medicinal iron gives better results when used intermittently than when used continuously, which indicates that the action is due to stimulation rather than to the inorganic iron actually going to form hemoglobin.

The results obtained by Tartakowsky* were more favorable to the view that hemoglobin may be formed from inorganic iron. He found that young growing animals fed on rice and milk gradually became anemic and finally ceased to grow; but that when inorganic iron was added to the rice-milk diet the blood regained its normal iron content and the animal soon began to grow again. From such experiments together with a large number of microchemical observations, Tartakowsky concludes that medicinal (inorganic) iron is assimilated like food iron and serves in the same way for the production of hemoglobin and the other organic iron compounds of the body. He further insists that Abderhalden's experiments should also be interpreted in the same way, since in many cases the animals which received inorganic iron in addition to their food formed more hemoglobin than the control animals.

More recently, Schmidt† has described some interesting experiments upon mice with a similar iron-poor rice-and-milk diet. According to Schmidt this diet did not cause anemia in adult mice; but the offspring of mice which had been kept on such diet seemed to lack the normal reserve store of iron, and by continuing the milk-rice diet to the third generation there were obtained what this investigator describes as "iron-free families" of mice. In these the red blood cells were very poor in hemoglobin. From such a family of mice two sisters seven months old were selected; one was continued on the milk-rice diet alone while the other was fed medicinal iron (Ferrum oxydatum saccharatum) in addition for eleven days; then both were killed and examined. The first showed the typical anemic condition of these "iron-free families," the hemoglobin number and number of red blood cells being both less than half of the normal; while in the second mouse, which had received medicinal iron for eleven days, the hemoglobin number and number of red blood cells were both about twice as high as in the first. This is held by Schmidt to show that medicinal iron does not merely stimulate the blood-forming organs to greater activity but does itself enter into hemoglobin formation.

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* *Archiv für die gesamte Physiologie,* Vol. 100, page 586; Vol. 101, page 423 (1903, 1904).

† *Verhandlungen der Deutsches Pathologisches Gesellschaft,* Vol. 15, page 91 (1912).

It is difficult to determine how much weight should be given to the findings of Tartakowsky and of Schmidt as opposed to the more extended and more quantitative experiments of Häusermann and of Abderhalden.

While it cannot yet be stated positively that inorganic iron is or is not used by the animal body as material for the production of hemoglobin, the best medical opinion appears to support the conclusion reached by Abderhalden, that hemoglobin is derived essentially from the organic iron compounds of the food, while inorganic iron acts mainly if not entirely as a stimulus. This view is strongly supported by Von Noorden in his treatise on chlorosis in Nothnagel's *Encyclopedia of Practical Medicine*, and Ehrlich and Lazarus, writing on anemia in the same work, state:

"It is not very probable that the (medicinal) iron stored by the liver and spleen is directly employed in the formation of hemoglobin; on the contrary, the assumption first suggested by Von Noorden seems much more plausible, namely, that the iron exercises a direct irritative action on the function of the blood-making organs."

The Iron Requirement of the Body

A very brief summary of the leading facts regarding the normal nutritive relations of iron may well precede the discussion of the amount required.

Iron is an essential element of hemoglobin and of the chromatin substances, *i.e.* of the body constituents most directly concerned with the processes of oxidation, secretion, reproduction, and development. The substances thus fundamentally connected with metabolism processes contain their iron in firm organic combination, as a constituent of their characteristic proteins; and the normal materials for the production of these body constituents are the similar iron-protein compounds of the food.

The iron of the food is absorbed from the small intestine, enters the circulation by way of the lymph, and is deposited mainly in the liver, spleen, and bone marrow. Its final elimination takes place mainly through the walls of the intestines.

Both inorganic and synthetically prepared organic forms of iron are absorbed from the same part of the digestive tract, stored in the same organs, and eliminated by the same paths as the iron of the food. These medicinal forms of iron often stimulate the production of hemoglobin and red blood corpuscles.

Whether medicinal iron actually serves as material for the construction of hemoglobin is not positively known, but we have what appears to be good evidence that food iron is assimilated and used for growth and for the regeneration of hemoglobin to much better advantage than are inorganic or synthetic forms, and that when medicinal iron increases the production of hemoglobin, its effect is more beneficial in proportion as the food iron is more abundant — a strong indication that the medicinal iron acts by stimulation rather than as material for the construction of hemoglobin.

Evidently, then, we should look to the food rather than to medicines or mineral waters for the supply of iron needed in normal nutrition.

Comparatively few experiments upon the amount of food iron required for the maintenance of equilibrium in man have been made. Cetti and Breithaupt eliminated 0.0073 and 0.0077 gram per day, respectively, when fasting. Three men observed by Stockman while receiving in the food about 0.006 gram each per day eliminated 0.0063, 0.0093, and 0.0115 gram, respectively. Von Wendt found his requirements to range in a number of experiments on different diets from 0.008 to 0.016 gram per day, the largest amount being required in a case where the diet was deficient in calcium. In three experiments by Sherman in which the food contained 0.0057 to 0.0071 gram of iron there was metabolized 0.0055, 0.0087, and 0.0126 gram per day, respectively, and here also the amount of iron which sufficed for equilibrium when taken in the form of bread and milk (a diet rich in calcium) was insufficient when taken in the form of a diet (poor in calcium) consisting of bread and egg white, or bread alone. In this case, however, the difference in the economy of the metabolism of the iron may have been due not simply to the change in the calcium content of the food, but also to a superior nutritive value of the iron compounds of milk over those of bread and to the fact that the general conditions of digestion and nutrition were better when milk was included in the diet than when it was excluded. The nitrogen, phosphorus, calcium, and iron balances for two of these experiments performed upon the same man and with diets practically alike in energy value and protein content, are shown in the following table:

COMPARISON OF BALANCES OF DIFFERENT ELEMENTS

NATURE OF DIET	NATURE OF ELEMENT	AMOUNT IN GRAMS PER DAY			
		In food	In feces	In urine	Balance
Bread and milk . .	Nitrogen	10.10	0.46	13.09	− 3.45
Bread and egg white.	Nitrogen	10.69	0.75	13.21	− 3.27
Bread and milk . .	Phosphorus	1.55	0.57	1.03	− 0.05
Bread and egg white .	Phosphorus	0.38	0.22	0.75	− 0.59
Bread and milk . .	Calcium	1.89	1.34	0.15	+ 0.40
Bread and egg white	Calcium	0.10	0.34	0.07	− 0.31
Bread and milk . .	Iron	0.0057	.0053	.0002	+ .0002
Bread and egg white .	Iron	0.0065	.0085	.0002	− .0022

Here, although the nitrogen balance was practically alike on the two diets, there was on the bread and milk diet practical equilibrium of phosphorus and iron and a storage of calcium, while on the diet of bread and egg white there were noteworthy losses of all three of these elements.

Returning to the problem of the quantitative determination of the iron requirement it will be seen that in the cases in which the intake and output of iron have been determined, the requirement appears to have varied with individuals and with the nature of the diet from 0.006 to 0.016 gram (6 to 16 milligrams) of iron per man per day.

We might conclude from these results that a daily allowance of 10 to 12 milligrams of food iron should suffice for the maintenance of iron equilibrium in an average man under favorable conditions, but until the conditions which determine a larger metabolism of iron are more clearly defined, it would seem desirable to set a higher standard, perhaps 15 milligrams of food iron per man per day.

In calculating the iron requirement for a family dietary, it is well to make the allowance for women and children more liberal than would be indicated by their total food requirement. A woman requiring eight tenths as much food as a man will probably require more than eight tenths as much iron, and a child requiring half as much food may easily require more than half as much iron; for the influence of menstruation, pregnancy, and lactation in women and of growth and development in children may reasonably be expected to affect the demand for iron to an even greater extent than they affect the requirement for total food. It is probable that pregnancy and lactation increase the iron requirement of the mother by at least 3 milligrams per day, and at other times the losses of blood in menstruation must call for a greater intake of iron than would be needed by a healthy man of equal energy and protein requirement.

Since milk is the sole food of young mammals during a considerable period of rapid growth, Bunge was surprised to find only small amounts of iron in milk ash. Comparing the composition of the ash of milk with that of the newborn animals of the same species, it was found that, while other constituents occurred in nearly the same relative proportions, the iron was six times as abundant in the ash of the young animal as in that of the milk on which it was nourished. That the suckling animal grows rapidly and increases its blood supply in spite of this apparent deficiency of iron in its food is due to the fact that the body contains a reserve supply of iron at birth. In confirmation of this statement Bunge and his pupils have published many analyses showing that the percentage of iron in the entire organism is highest at birth, and that during the suckling period the amount of iron in the body remains about constant, notwithstanding the increase in body weight.

In all cases in which the young depend entirely upon the milk of the mother during the suckling period the body constituents of the young must evidently be derived entirely from the maternal organism either before birth through the placenta or after birth through the milk glands of the mother and the digestive tract of the young. Since disordered digestion may readily lead to defective absorption of the iron of the food, nature apparently takes the precaution of conveying the necessary iron from mother to offspring mainly by the safer method, *i.e.* through the placenta. Hence in the case of animals which feed solely upon milk for some time after birth, a relatively large amount of iron is stored before birth for use in the formation of hemoglobin during the suckling period. This has been shown by analysis to be true of children, puppies, kittens, and rabbits. On the other hand, guinea pigs, which feed on green leaves or other food rich in iron from the first day of life, are born without this reserve store of iron (Bunge). From recent analyses it appears that the percentage of iron in the human body is about three times as high at birth as at maturity. If it be assumed, as indicated by Bunge's work, that during the milk feeding of infancy the amount of iron in the body remains about constant, it would follow that the percentage of iron in the child's body would be reduced to that in the adult when the body weight becomes about three times what it was at birth — usually when a little over one year old, — and that from this time on throughout the period of growth, care should be taken that the food is sufficiently rich in iron to provide not only for equilibrium, but also for the constantly increasing blood supply.

Iron in Foods

Little weight can be attached to such statements regarding the iron content of foods as are based upon the data obtainable from the ordinary tables of ash analyses, since these have usually been obtained by methods which are likely to greatly overestimate the amount of iron. In the following table are shown the approximate amounts of iron now believed to be present in the average edible portion of typical food materials expressed (1) in milligrams per 100 grams of edible material, (2) in milligrams per 100 grams of protein, (3) in milligrams per 3000 Calories:

IRON IN TYPICAL FOOD MATERIALS

Food	Iron per 100 Grams Fresh Substance, Milligrams	Iron per 100 Grams Protein, Milligrams	Iron per 3000 Calories, Milligrams
Beef, all lean	3.85	16	97
Beefsteak, medium fat	2.2	16	47
Eggs	3.0	22	57
Egg yolk	8.6	53	69
Milk, whole	0.24	7	10
Milk, skimmed	0.25	7	20
Cheese	1.3	5	9
Oatmeal	3.8	22	26
Rice, polished	0.9	11	7
White flour	1.0	7	7
Wheat, entire grain	5.0	37	42
Beans, dried	7.0	40	60
Beans, string, fresh	1.1	48	80
Beets	0.6	38	39
Cabbage	1.1	69	104
Carrots	0.6	55	40
Corn, sweet	0.8	26	23
Peas, dried	5.7	23	46
Potatoes	1.3	55	42
Spinach	3.6	135	450
Turnips	0.5	39	38
Apples	0.3	78	15
Bananas	0.6	47	18
Oranges	0.2	25	12
Prunes, dried	3.0	143	30
Almonds	3.9	19	18
Peanuts	2.0	8	11
Walnuts	2.1	11	9

Percentages of iron in some other foods will be found in the tables of ash constituents in the Appendix. Using these recent data for iron in food materials, approximate estimates of the amounts of iron contained in 150 American dietaries have been made. The majority of these were found to furnish 14 to 20 milligrams of iron per man per day. Apparently therefore the typical American dietary does not contain any such surplus of iron as would justify the practice of leaving the supply of this element entirely to chance. The available data rather indicate that foods should be selected with some reference to the kinds and amounts of iron compounds which they contain.

Meats. — In meat as ordinarily eaten the iron exists largely as hemoglobin, due to the blood contained in the muscular tissue as usually sold and prepared for the table. Muscular tissue washed free from blood contains iron, but the amount is comparatively small. Since fatty tissue contains much less iron, the iron content of fat meat is much lower than that of lean, and in order to establish any useful estimate of the amount of iron in meat it is practically necessary to consider the lean tissue alone or to refer the iron to the protein content rather than to the gross weight of the meat. When expressed on the former basis, the results will still be influenced by the extent to which the blood has been either accidentally or intentionally removed from the muscle.

For fresh lean beef containing the full proportion of blood, the results obtained by most investigators are in satisfactory agreement, and the average figure, 0.00375 per cent iron in the fresh meat free from visible fat, can be accepted with little danger of serious error. This corresponds to about 15 to 16 milligrams of iron per 100 grams of protein in beef, and since no certain differences in iron content in the flesh of different species have been shown, it is assumed for the present that approximately the same ratio of iron to protein will hold for meats in general.

The iron of meat, as already mentioned, is largely due to the blood retained in the muscular tissue. The nutritive value of blood is often questioned. So far as the iron compounds of the blood are concerned, it seems to be established that hemoglobin and hematin may be absorbed and assimilated to some extent, but probably not to such good advantage as the iron compounds of eggs, milk, and vegetable foods.

Eggs. — The edible portion of hens' eggs has shown as the average of several analyses 0.00303 per cent of iron. Whether the iron content of eggs can be increased by giving to poultry food rich in iron, is a disputed question.

There can be no doubt regarding the assimilation and utilization of the iron compounds of eggs, since they serve for the production of all the iron-holding substances of the blood and tissues of the chick, there being no possibility of the introduction of iron from without during incubation.

Milk. — Analyses of samples of cow's milk of various origin have given results varying from 0.0002 to 0.0003 per cent, and averaging 0.00024 per cent of iron in the fresh substance.

It cannot be doubted that the iron of milk is readily absorbed and assimilated, since this constitutes the sole natural source of iron for all young mammals during a period of rapid growth. Moreover, metabolism experiments indicate that the iron of milk is likely to be utilized to especially good advantage, perhaps on account of its association with a high proportion of calcium.

The question of the iron supply of infants fed upon diluted or modified cow's milk may, however, be considered at this point. It is now generally recognized that the best substitute for mother's milk is obtained by diluting whole cow's milk or top milk with a solution of lactose or maltose. By varying the richness of the milk or top milk used and the amounts of water and sugar added, the composition of the modified milk can be controlled at will. In order to ascertain whether the iron compounds of milk tend to condense upon the fat globules or for any other reason are altered in their distribution by the rising of the cream, a sample of milk was allowed to stand, and after the cream had risen, the iron and nitrogen contents were determined separately in the upper half, containing all of the cream, and in the lower half, which consisted of skimmed milk. These analyses showed in the upper half 0.000277 per cent of iron and 0.54 per cent of nitrogen; in the lower half 0.000293 per cent of iron and 0.59 per cent of nitrogen. It is evident, therefore, that the ratio of iron to nitrogen was practically the same in the cream as in the milk. It is therefore important to recognize that the iron content of cow's milk is little if any higher than that of human milk, while the protein content is at least twice as high; that any modification of cow's milk which reduces its protein content will reduce the iron content in practically the same proportion, and that an infant fed upon cow's milk, modified or diluted to contain less than 3 per cent of protein, is probably receiving food poorer in iron than human milk. According to present estimates an infant fed on any modification of cow's milk must consume the equivalent of nearly a quart of undiluted milk or cream in order to obtain as much iron as is supplied daily in the milk of the average healthy nursing mother. Since no such quantity of cow's milk can safely be fed in early infancy, it is to be expected that during the first months of life the artificially fed infant will use up the surplus store of iron with which it was born more rapidly than will the child of the same age which receives the milk of a healthy mother.

Grain products. — Iron in combination with protein matter is found in considerable quantity in the cereal grains, but the greater part of it is in the germ and outer layers, and so is rejected in the making of the "finer" mill products, such as patent flour, polished rice, and new-process corn meal. In view of the part which the iron of the germ takes in the sprouting of the seed and the nutrition of the young plant, there is little room for doubt that it is of value also in the animal economy. To test the value of the iron in the outer layers of the grain Bunge * carried out the following experiment:

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* *Zeitschrift für physiologische Chemie*, Vol. 25, page 36 (1898).

A litter of eight rats was divided into two groups of four each, one group fed upon bread from fine flour, the other upon bread made from flour including the bran. At the end of the fifth, sixth, eighth, and ninth weeks, respectively, one rat of each group was killed, and the gain in weight, the total amount of hemoglobin, and the percentage of hemoglobin in the entire body were determined. The average results were as follows:

EFFECT OF FEEDING DIFFERENT KINDS OF BREAD ON GROWTH AND IRON CONTENT OF BODY IN EXPERIMENTS WITH RATS

KIND OF RATION	GAIN IN WEIGHT OF BODY	TOTAL HEMOGLOBIN IN BODY	PROPORTION OF HEMOGLOBIN IN BODY
	Grams	Grams	Per cent
White bread	4.81	0.2395	0.613
Bran bread	20.76	0.3492	0.714

Here the bran-fed rats not only made a much greater general growth, but developed both a greater amount and a higher percentage of hemoglobin. There can be no doubt that the iron and other ash constituents of the outer layers of the wheat were well utilized in these cases.

Vegetables and fruits. — Not many direct studies upon the iron compounds of the fruits and vegetables have been made, but Stoklasa has separated from onions an iron-protein compound very similar to the hematogen obtained by Bunge from egg yolk, but containing a considerably higher proportion of iron. Preparations similar in properties were also obtained from peas and from mushrooms.

In view of the fact that the herbivorous animals, which are less liable to anemia than the carnivora, obtain their normal food iron entirely from vegetable sources there is every reason to suppose that man makes good use of the iron of the fruits and vegetables in his diet. Moreover, since (as Herter has shown) anemic conditions and excessive intestinal putrefaction often go together, the bulkiness and laxative tendency of fruits and vegetables, along with their relatively high iron content, are advantageous in combating the conditions which give rise to excessive putrefaction, and at the same time increasing the supply of food iron.

Among typical food materials omitted from the above table because of containing little if any iron, may be mentioned fat pork, bacon, lard and suet, butter, salad oil, sugars, starches, and confectionery. All of these foods have high fuel value, and many are economical and highly important elements in a normal dietary. Excessive use of these foods, however, would tend to satisfy the appetite and supply the body with the needed fuel without furnishing the desirable amount of iron. On the other hand, the fruits and fresh vegetables are often regarded as of low nutritive value because of their high water content and low proportions of protein and fat. But it is largely this property which makes them especially important as sources of food iron, because they can be added to the diet without replacing the staple foods of high calorific and protein value, and without making the total food consumption excessive. Thus the above table shows plainly that the ratio of iron both to protein and to fuel value is high in nearly all of the typical fruits and vegetables, so that in most cases it would be necessary to increase only slightly the amount of protein and fuel value derived from these sources, in order to effect a material increase in the iron content of the dietary. The iron content of eggs is also high, but the cost of these is often such as to restrict their use in families of limited means, while present methods of drying and preserving tend to equalize the cost and increase the available variety of fruits and vegetables throughout the year. The ratio of iron to fuel value is also high in lean meat, but here, as has already been pointed out, the iron exists largely in the form of hemoglobin, which appears to be of distinctly lower nutritive value than the iron compounds of milk, eggs, and foods of vegetable origin. Especially in families where there are young children it would be a mistake to rely too largely upon meat as a source of iron. Von Noorden, who is one of the strongest advocates of a liberal use of meat in the adult dietary, says in regard to the feeding of children:

"The necessity of a generous supply of vegetables and fruits must be particularly emphasized. They are of the greatest importance for the normal development of the body and of all its functions. As far as children are concerned, we believe we could do better by following the dietary of the most rigid vegetarians than by feeding the children as though they were carnivora, according to the bad custom which is still quite prevalent. . . . If we limit the most important sources of iron, — the vegetables and the fruits, — we cause a certain sluggishness of blood formation and an entire lack of reserve iron, such as is normally found in the liver, spleen, and bone marrow of healthy, well-nourished individuals."

In an experimental dietary study made in New York City it was found that a free use of vegetables, whole wheat bread, and the cheaper sorts of fruits, with milk but without meat, resulted in a gain of 30 per cent in the iron content of the diet, while the protein, fuel value, and cost remained practically the same as in the ordinary mixed diet obtained under the same market conditions.

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CHAPTER XII

ANTISCORBUTIC AND ANTINEURITIC PROPERTIES OF FOOD

RECENT investigations have shown that food furnishing sufficient amounts of proteins, fats, carbohydrates, and inorganic foodstuffs may not always prove permanently adequate. Some at least of the food materials which go to make up a completely adequate diet must have properties beyond those which have been considered in the preceding chapters. For the present these additional properties are best expressed in terms of their physiological effects. The term "deficiency diseases" has been introduced as a designation for those disorders which are thought to be due to dietary deficiencies of this sort, and the nature of the disorder arising from the use of any given diet serves to designate the property which has to do with the cause or prevention of the disease. Scurvy and beriberi have in recent years been considered the typical deficiency diseases. In normal nutrition the occurrence of scurvy is prevented by the *antiscorbutic* properties of the food. Beriberi is primarily a disease of the nerves, a neuritis, and can be prevented by the use of food adequate in *antineuritic* substances or properties. Similarly some foods have *growth-promoting* properties beyond what can be accounted for by the proteins, fats, carbohydrates, and salts which they contain.

As our knowledge in this field is not yet sufficiently developed to permit a satisfactory chemical classification of the subject matter, the antiscorbutic and antineuritic properties of foods will be considered in this chapter, and the growth-promoting properties in the next. The reader should keep clearly in mind the fact that these are matters of active investigation at the present time so that even while this is being printed, new results tending to modify our views on these subjects may appear. The present text is written chiefly in the light of such investigations as were available in May, 1917.

Scurvy and the Antiscorbutic Property of Food

For centuries scurvy was one of the most common diseases in Europe and at times among people of European races in North America. It was most frequent and most severe in the more northern regions, where the people were often confined to a limited and monotonous diet of bread or other grain products and meat or fish through a large part of the year. As a rule fruits and vegetables were eaten only during their short natural season.

On the long voyages which followed the discovery of America, sailors were often obliged to subsist for many months at a time on food even more restricted in variety than that of the winter diet of Europe because they were cut off not only from supplies of fresh fruits and vegetables but also from fresh meat. Their food supplies thus often consisted essentially of breadstuffs and salted meats. On such voyages there were many exceedingly severe outbreaks of scurvy and it gradually came to be recognized that scurvy might be expected when men were kept for a long time on diets which lack fresh food.

The European sailors whose experiences on their long voyages to America did so much to establish the relationship between diet and scurvy and the fact that fresh foods, particularly fresh fruits and vegetables, have antiscorbutic properties, were also instrumental in bringing about a great diminution of the disease. They introduced into Europe from America the cultivation of the potato and since that time, as potato culture and the use of potatoes as food throughout the year have become more common in Europe, scurvy has become less common.

For the past two or three generations serious epidemics of scurvy among adults have not often occurred except as the result of crop failure, imprisonment with inadequate food supply, or siege.

In all such cases of which we have accurate accounts the common feature appears to be the lack of potatoes or other fresh vegetable or fruit in the diet. Scurvy on shipboard is now avoided by carrying more liberal quantities of potatoes among the rations, and, in case of long voyages, the juice of lemons or limes is taken specifically for its antiscorbutic properties.

Garrod called attention to the fact that foods shown by experience to have good antiscorbutic properties (potatoes, lemon and lime juices, fruits and vegetables generally) are rich in potassium; and suggested that the cause of scurvy may be too small an intake of potassium — particularly of " acid vegetable potassium " convertible into potassium carbonate on oxidation.

However, the tendency of scurvy to occur epidemically (as well as some other pathological features) has also seemed suggestive of a bacterial origin and Litten after weighing the evidence available in the early years of this century wrote:* " However fascinating the potassium theory may be, it is by no means absolutely proven, and it does not contradict the view that scurvy may, in spite of this, be an infectious disease. Scurvy may perhaps be assumed to be an infectious disease of a non-contagious nature produced by a microörganism which finds in a body deficient in potassium a favorable culture medium for its development."

Wright, impressed with the fact that experience has shown scurvy to develop in cases in which the diet contains a preponderance of "acid forming" foods such as bread and meat, while foods of high antiscorbutic value, *i.e.* fruits and vegetables, are such as yield alkaline ash, was led to advocate the view (held also by Gautier) that the cause of scurvy is a sort of acidosis due to the constant production of a relative excess of acid in metabolism. An outbreak of the disease among the English soldiers besieged in Ladysmith during the Boer War gave Wright an opportunity to test his views and he found that in the scurvy patients the "titration alkalinity" ("alkali reserve") of the blood was considerably below normal and that by feeding sodium or potassium salts of organic acids such as acetate, citrate, or lactate he was able to effect a rapid improvement both in the scurvy symptoms and in the blood alkalinity.

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* Cabot's *Diseases of Metabolism* (translation from *Die Deutsche Klinik*), p. 399.

Holst and Fröhlich, studying experimental scurvy in guinea pigs, find that some foods such as cabbage show a marked loss of antiscorbutic power as the result of simple heating or slow drying, while others (grains) develop antiscorbutic value in sprouting. In neither of these cases is the relation of acid-forming to base-forming elements altered and these authors therefore consider that they have entirely disproven the acidosis theory of Wright and that antiscorbutic properties of foods have no connection with their ash constituents but are due to the presence of small quantities of a specific organic substance or substances, of undetermined chemical nature, and (in most cases at least) very readily destroyed by heat.

Guinea pigs fed exclusively on bread or grain developed symptoms which Holst and Fröhlich considered to be "identical in all essentials with those of human scurvy." Since one of these symptoms is loss in weight and since animals may fail to eat enough of a one-sided diet to meet the energy requirement, special experiments were made to establish the distinction between the effects of scurvy and those of starvation or undernutrition. It was found that guinea pigs kept on an exclusive diet of fresh raw cabbage, dandelion greens, or even carrots may die of starvation; but they do not become scorbutic. Those kept on grain alone regularly became scorbutic. Those fed grain plus a moderate allowance of cabbage, dandelion, carrot, potato, or other fresh vegetable remained normal. The antiscorbutic properties of other foods were then tested by adding them to a bread or grain diet and observing whether the guinea pigs developed symptoms of scurvy or not.

Raw cabbage, dandelion greens, lettuce, endive, sorrel, potatoes, carrots, bananas, apples, and cloudberries all showed antiscorbutic properties — apparently in varying degrees. Apples and bananas were thought to be somewhat less effective than the potatoes, lettuce, greens, and berries. Cabbage and dandelion juices seem to lose their antiscorbutic properties more rapidly than the vegetables themselves. Fruit juices and sorrel juice on the other hand retain their efficacy as antiscorbutics remarkably well. Raspberry juice seemed but little injured by heating for 1 hour at 100° or even 110°. Acidulated cabbage or dandelion juice retained its antiscorbutic property much better than the natural juice of these vegetables. If, as these experiments indicate, the antiscorbutic property is due to the presence of some unstable substance, the latter would appear to be much more stable in an acid than in a neutral or alkaline medium.

The effect of cooking was studied in the case of several different foods with the following results: Cabbage cooked at 100° for ½ to 1 hour was still a good antiscorbutic. Carrots cooked at 100° for 1 hour showed a great diminution in antiscorbutic power. Cooking for ½ hour at the same temperature showed a less serious injury to the antiscorbutic property. Cauliflower was much injured by cooking for 1 hour at 100°; when cooked only ½ hour it was a much better antiscorbutic. Dandelion leaves lost much of their antiscorbutic property when cooked for 1 hour at 100°. Potatoes cooked at 100° "in the usual way" (½ hour) had excellent antiscorbutic properties.

Turnips and kohlrabi cooked at 100° had antiscorbutic power similar to cooked potatoes. Cloudberries retained their efficiency after cooking to a very marked degree. When cooked at 100° as usual they were still excellent antiscorbutics and were shown to retain this property when kept for at least 3 months after cooking. From this it would appear that canned fruit which has been sterilized at temperature of boiling water and then kept in a cool place ought to be a good antiscorbutic even after many months, and in general that ordinary cooking of vegetables (or low temperature pasteurization of milk) destroys only a part of the antiscorbutic substance, and so the food still possesses antiscorbutic properties though not in as high degree as when raw.

The results of several recent investigations are, however, not entirely consistent with the findings of Holst and Fröhlich.

Funk, who had been a prominent advocate of the theory that scurvy is due to deficiency of a specific unidentified substance, has recently concluded that the disease produced in guinea pigs by a diet of oats (Holst and Fröhlich's experimental scurvy) may be due to acidosis. It has also been found independently by Jackson and by McCollum that guinea pigs are so susceptible to nutritive disorders with scurvy symptoms when placed upon experimental diets as to make the interpretation of such experiments exceedingly difficult. Jackson finds in the scorbutic tissues of the experimental animals bacteria of the *Diplococcus* type which appear to be specific to the scurvy lesions and pathogenic when inoculated into other guinea pigs. The results of such inoculation depend largely upon the diet; guinea pigs fed on carrots, cabbage, and hay appear relatively immune, while those fed on grain or bread diet are much more susceptible. According to McCollum the physical character of the diet and of the resultant intestinal residues is responsible for guinea pig scurvy. His examinations of guinea pigs dying with scurvy symptoms reveal characteristically an abnormal accumulation of fecal material in the cæcum. McCollum holds that the guinea pig will have scurvy on any diet which does not contain a succulent vegetable and that this is due to the anatomical character of the digestive tract, the cæcum being relatively large and delicate in this species and especially liable to the accumulation of fecal residues when the food is not of suitable physical character. His guinea pigs showing typical scurvy symptoms recovered after liberal doses of petroleum oil. He therefore holds that guinea pig scurvy, although " referable to faulty diet, " is not a deficiency disease, the fault lying rather in the unsatisfactory physical character of the diet which leads to an injurious accumulation of material in the cæcum. The immediate cause of the pathological symptoms of scurvy is not known. It may perhaps be due to absorption of toxic substances resulting from bacterial action in the cæcum or to invasion of bacteria through an injured intestinal wall. In view of these results so recently reported by McCollum it becomes extremely difficult to interpret the work of Holst and Fröhlich, who apparently failed to realize the part played by such digestive disorders.

It also remains an open question whether guinea pig scurvy and human scurvy are referable to the same causes.

Recently, as a result of war conditions, there has been renewed interest in human scurvy and a tendency toward the view that this may be a disease in which two factors, a nutritional condition and an infection, may both be involved.

It also seems probable that the term "scurvy" may have been applied to more than one disease in man.

Infantile Scurvy (Barlow's Disease)

An investigation conducted by the American Pediatric Society in 1898 showed that infants developing scurvy had in nearly all cases been fed with heated milk or with proprietary foods.

Infantile scurvy is usually quickly cured by feeding either raw milk, or milk which has been pasteurized at a low temperature supplemented by some fresh fruit juice (usually orange juice).

Investigations to determine whether children are subject to scurvy when fed exclusively upon pasteurized milk have given conflicting results, probably for two reasons: (1) pasteurization of the milk at different temperatures or for different lengths of time in different cases, (2) differences in susceptibility to scurvy among infants.* Aging of the milk may also be a factor (Hess).

Hess and Fish report that they have had a considerable number of cases of infantile scurvy among hospital children fed on milk pasteurized at 145° F. for 30 minutes or 165° F. for 20 minutes. Orange juice was efficient as a preventive or cure and did not lose its antiscorbutic property when boiled for 10 minutes. It was found that the juice of the orange peel could be substituted for that of the orange as an antiscorbutic. Potato was found to be an excellent antiscorbutic for children, and the authors propose that potato water (made by mixing a tablespoonful of boiled potato in a pint of water) be used as a diluent instead of the barley water now commonly used in modifying cow's milk for infants. They held that if this is done, no other antiscorbutic will be necessary.

In his later papers (1915, 1916), Hess reports that when milk which has been heated for 30 minutes at 145° F. is fed with sugar and cereal, but without orange juice or other antiscorbutic food, for from two to eight months there is usually a development of mild scorbutic symptoms, or a subacute scurvy such as might pass unrecognized. Such cases are apt to show some but not all of the classical symptoms of infantile scurvy and usually involve retardation of growth. Under these conditions the addition of an antiscorbutic food such as orange juice to the diet induces an increased rate of growth as well as relief of such other scorbutic symptoms as may have developed. Even if, as some critics have suggested, the symptoms reported by Hess are somewhat different from those shown by well-developed and clearly marked cases of infantile scurvy, the influence which the presence or absence of antiscorbutic food in the diet was shown to exert upon the nutrition and rate of growth of the infant is a matter of considerable interest from the standpoint of food chemistry.

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* Differences in susceptibility to scurvy are to be expected in view of the well-known fact that when groups of men, as sailors and prisoners, are subjected to the same conditions and partake of the same rations, some become scorbutic while others do not. Physicians have also found that some infants show signs of scurvy when receiving an amount of antiscorbutic food which is amply sufficient for most infants and recover when a diet still richer in antiscorbutics is given.

More recently still (1917), Hess finds that infantile scurvy is possibly not a single disease, and probably not a simple dietary disease. Use of pasteurized milk is a contributing cause, but the aging of such milk is quite as much a factor as the heating. The diet is held to be at fault in allowing the intestinal bacteria to elaborate toxins, while antiscorbutic foods improve intestinal conditions and are also beneficial as diuretics.

Antineuritic Properties of Food

Our knowledge of the antineuritic properties of foods has been obtained through the study of beriberi in man or of experimental beriberi in fowls or pigeons. While the symptoms of beriberi are variable the disease is chiefly characterized by degeneration of the nerves beginning with those of the extremities (" polyneuritis," " multiple peripheral neuritis ").

For a long time beriberi was very common in the Orient (Malay States, Siam, parts of Japan and the Philippines) and in recent years beriberi has also been found in Newfoundland and Labrador. Cases are also occasionally reported from the southern and western parts of the United States.

Takaki, while Inspector General in the Japanese Navy, was much disturbed at the large proportion of men who suffered from beriberi, and in 1880 began a systematic investigation which indicated that the frequency of the disease was more closely connected with the nature of the food than with any other probable factor since climate was found to be without influence and the sanitary conditions on the Japanese ships were as good as those in the European navies which were not troubled with the disease.

A Japanese naval vessel with 276 men on a 9 months' cruise from Japan to New Zealand, Valparaiso, and Honolulu had 169 cases with 25 deaths. Another vessel with a similar crew was sent by Takaki over the same route with a ration in which the rice was decreased, the barley increased, and vegetables, meat, and condensed milk added. In this case only 14 men had beriberi and each of these had failed to eat his full allowance of the new foods. As the result of this experiment Takaki secured the adoption of his new ration for the entire Japanese navy with the result that the number of cases of beriberi soon became practically negligible.

Takaki attributed this to the fact that the new diet was richer in protein, having a ratio of 1 part nitrogen to 16 parts carbon, whereas the old ration had only 1 part nitrogen to 28 parts carbon. The great reduction in beriberi was undoubtedly due to the change of diet, but not primarily to the increased protein intake. Apparently because the explanation available at the time was not sufficiently convincing, Takaki's great achievement was not fully appreciated, and medical opinion continued for several years to regard beriberi as possibly an infectious disease. But no success attended the attempts to check the disease by sanitation, while indications that the cause might be nutritional continued to be found.

In 1907 Braddon published in his book, "The Cause and Prevention of Beriberi," a large amount of evidence connecting the disease with the eating of polished rice.

At about the same time Fletcher, by experimenting with the diet in a lunatic asylum, showed that when 28 oz. of rice was fed daily with only small amounts of other food, the use of polished or unpolished rice was alone sufficient to determine the occurrence or non-occurrence of beriberi.

During 1907–1908 Fraser and Stanton took 300 laborers from Java into new and sanitary quarters in a virgin jungle and demonstrated in striking fashion that with rice as the main part of the diet, beriberi followed the use of polished but not of unpolished rice. Many other observations to the same effect were also published at about this time.

In 1909, convinced that beriberi was related to diet, the U. S. Army Medical Commission in the Philippines initiated changes in the rations of the " Philippine Scouts " and in 1911 Chamberlain was able to announce the eradication of the disease from these troops by the substitution of unpolished rice (and a small quantity of beans) for the polished rice previously used. Until the year 1910, the number of hospital cases of beriberi ranged from 115 to 618 (the force numbering about 5000 men). During 1910 changes in the dietary were begun and that year the cases dropped to 50. In 1911 there were 3; in 1912, 2; in 1913, none; in 1914 up to June 30 (date of latest available report) there was 1.

In 1908–1909, when beriberi was at its worst among the Scouts, the diet consisted essentially of 12 oz. of beef, 8 oz. of white flour, 8 oz. of potatoes, and 20 oz. of rice (ordinarily polished). The change in the ration, as finally decided upon after some months of experimentation, consisted in giving, in place of the 20 oz. of polished rice, 16 oz. of unpolished rice and 1.6 oz. of dried beans. Experiments, made largely upon fowls as explained below, have shown that while meat has some effect in preventing beriberi, an equal weight of beans, peas, or peanuts is much more efficacious.

A further improvement could have been made by substituting some whole grain product for the white flour since it is now known that a diet consisting too largely of white flour or bread may in itself be a cause of beriberi; * but this appeared unnecessary inasmuch as the changes already noted sufficed to eradicate the disease.

Chamberlain states, in fact, that the disease had disappeared as the result of adding the beans to the ration, before the substitution of unpolished for polished rice had been completed. He believes " that the consumption of beans to the daily amount of 1.6 ounces would, unaided, have prevented a recurrence of beriberi, but it would obviously be difficult to make sure that all the men ate their share of this article over long periods, and it is therefore much safer that the largest component of the diet, the rice, should be of the unpolished variety and by itself sufficient to prevent neuritis."

Several other investigations gave similar results. These repeated demonstrations of a close connection between a diet consisting too largely of polished rice and the occurrence of beriberi naturally gave a great impetus to experiments designed to find what constituents of the rice are directly concerned in the disease.

Attempts to Isolate an Antineuritic Substance

Such experiments were greatly facilitated by the fact, discovered by Eijkmann in 1897, that fowls develop a diseased condition closely resembling beriberi in man, when they are fed exclusively upon polished rice for 3 or 4 weeks. Ohler (1914) finds that an exclusive diet of white bread, especially when made without yeast, has the same effect as the polished rice diet. This experimental beriberi of fowls (or " polyneuritis gallinarum ") does not occur when whole rice or even rice which has been partially milled so as to retain the inner bran

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* Little (1914). The prevalence of beriberi in Newfoundland and Labrador appears to be due to a diet too largely restricted to white bread.

coat (pericarp or " silverskin ") is fed. It was soon found that rice polishings (bran) when added to the polished rice diet not only protected the fowls but also cured those which had already developed the disease. Aqueous and alcoholic extracts of the rice polishings also served to prevent or cure the disease. The same was found true of many ordinary foods such as meat, potatoes, beans, peas, and peanuts, the legumes being especially efficient.

Aron working on Oriental beriberi in the Philippines, and Schaumann in Europe, centering his interest more particularly in ship beriberi, were both impressed with the fact that diets which cause beriberi are poor in phosphorus and that foods of good curative and preventive properties are rich in phosphorus. They were therefore inclined to regard beriberi as connected with a deficiency of phosphorus in the diet. Their attempts to prevent or cure the disease by adding definitely known phosphorus compounds to the polished rice diet gave, however, for the most part negative results. In Aron's experiments the deleterious effects seemed to be reduced though not excluded when phytin was fed. In Schaumann's experiments yeast lecithin and yeast nucleic acid seemed effective, but egg lecithin, phytin, simple phosphates, and glycerophosphate showed no beneficial results. The direct evidence for the " phosphorus theory " is therefore weak and somewhat conflicting. (This does not exclude the possibility that deficiency of phosphatids may be at least a factor in the nerve degeneration as argued by Schaumann.)

Furthermore, Fraser and Stanton showed that an extract of rice polishings which contained only 15 per cent of its total phosphorus was capable of preventing the neuritis, while the residue containing the other 85 per cent of the phosphorus was ineffective; and soon afterward Chamberlain and Vedder showed that an alcoholic extract of rice polishings which was highly protective contained only 0.0007 per cent of phosphorus or less than one part in one thousand of the phosphorus originally present in the polishings.

Chamberlain and his associates also tried the effects of various inorganic salts, of sugar, phytin, lecithin, allantoin, choline, and many of the amino acids, all of which proved insufficient to prevent the development of polyneuritis in fowls kept on a polished rice diet. On the other hand, they added to the knowledge of the properties of the antineuritic substance by a study of the effectiveness of rice bran extracts after different treatment. The antineuritic substance was found to be insoluble in ether but soluble in alcohol or in water and dialyzable. It was not volatile but was destroyed by heating or by alkali; in the presence of acid, it was more stable. It was not precipitated by lead acetate. They held the curative substance to be an organic base but not an alkaloid. Bean extracts were found to contain one or more substances having similar properties. Fresh milk, meat, and potatoes were also found to have antineuritic properties.

Later in 1911 and early in 1912, several investigators independently and almost simultaneously succeeded in isolating what appeared to be specific antineuritic substances.

Funk's experiments, begun about the middle of 1911, have attracted special attention since he was the first to announce (December, 1911) the isolation of a definite chemical substance possessing the antineuritic property. Pigeons paralyzed by neuritis induced by a polished rice diet were able to run and fly within a few hours after administration of 2 to 8 milligrams of this substance, which appeared to be an organic nitrogenous base related to the pyrimidines and to which Funk gave the name *vitamine*. He described the preparation of such substances from rice bran and from yeast, and inferred the existence of the same or a similar vitamine in all foods which have antineuritic properties. Funk's view of the relation of vitamine to the phenomena of beriberi is as follows: The lack of vitamine in the food forces the animal to get this substance from its own tissues (with the result that there is wasting of the muscles causing emaciation unless accompanied by œdema). After the stock of vitamines available in the muscles begins to be scarce, there results a breaking down of the nerve tissue and the appearance of nervous symptoms such as are observed in beriberi.

Funk called this *beriberi vitamine.* It constituted only 0.05 per cent of the rice polishings corresponding to about 0.01 per cent in the whole grain.

In March, 1912, Edie, Moore, Simpson, and Webster (working independently of Funk) described the isolation from yeast of a base which promptly cured pigeons suffering from polyneuritis. This base they described as having composition corresponding to the formula $C_7H_{17}N_2O_5$. They called it *toruline.*

Schaumann (June, 1912) reported the preparation of a phosphorus-free nitrogenous crystallizable base corresponding in general to the description given by Funk and exerting a marked restorative action upon polyneuritic pigeons. This base he considers the "activator" in the cure of polyneuritis, holding that it "mobilizes" the phosphatid substances which must be rebuilt into the degenerated nerve tissue in order to effect a permanent cure.

In July, 1912, Suzuki, Shimamura, and Odake, reported an extended investigation of experimental beriberi in which they had prepared from rice polishings by an independent method a base of high curative power which they called *oryzanine.* In preparing oryzanine they precipitated an alcoholic extract of rice polishings with tannin, decomposed the tannate by baryta, removed the barium by sulphuric acid, and precipitated the base as a picrate. Only 0.005 to 0.01 gram of oryzanine was required to make the daily diet of polished rice adequate for a pigeon. Since the pigeons ate 25 to 30 grams of rice per day this means that the oryzanine was only $\frac{1}{2500}$ to $\frac{1}{5000}$ of the (dry) weight of the food eaten. Feeding 0.3 gram cured a dog that was already paralyzed by experimental beriberi.*

It will be seen that these independent investigations all indicate that the antineuritic property shown by rice polishings, yeast, and other natural food materials is due to some basic nitrogenous substance or substances. Much work published since 1912 confirms this general view without establishing the chemical identity of either " Funk's base," or " toruline " or " oryzanine." Pending chemical identification of the naturally occurring antineuritic base or bases the term " vitamines " is commonly applied to them.

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* Apropos of the small quantities of vitamine or oryzanine necessary for pronounced effects, Lusk calls attention to the fact that epinephrine (adrenaline), an essential of life, is present in the blood to the extent of only 1 part in 100,000,000.

While the antineuritic property of such " vitamine " has been demonstrated usually by experiments upon animals, Williams and Saleeby have used a vitamine preparation, made from rice polishings, in a case of human beriberi with good results. In connection with this work it was found that acid hydrolysis renders the antineuritic substance of rice polishings more active, or more rapid in its action. It is possible that in natural food materials or simple water extracts the vitamine may exist, either wholly or in part, in combination. This would account for the greater activity and also for the instability of the free " purified " vitamine as compared with the natural form.

Seidell * has devised a method for obtaining a stable preparation of the antineuritic vitamine by precipitating it with hydrous aluminum silicate (Lloyd's reagent).

While the general view has been that a given organism requires a given amount of vitamine to maintain health (presumably a larger amount to effect recovery from disease induced by a previous deficiency), it was suggested by Braddon and Cooper (1914), and a few simultaneous experiments by Funk, that there is a connection between the metabolism of carbohydrate and of vitamine, so that the amount of antineuritic substance required by the organism increases with the quantity of carbohydrate metabolized.

It has also been suggested that the neuritis of beriberi is due to a toxic effect, upon the nerves, of some substance formed in, or absorbed into, the system and that the vitamine, when present in normal amounts, acts as a protection or antidote against such toxicity.

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* Reprint No. 325 from the Public Health Reports, U. S. Public Health Service.

This hypothesis is difficult to test and does not seem to have been much studied. Investigations designed to connect the physiological property with some definite chemical substance or type of molecular structure have, however, been continued and are yielding most interesting results.

Relation of Chemical Structure to Antineuritic Action

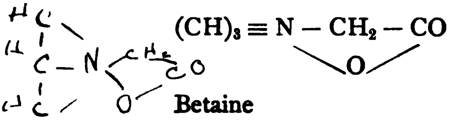
Williams has attacked this problem by synthesizing substances of known structure and testing them for curative action upon polyneuritic pigeons. Since such chemical examinations as had been made in connection with previous work upon active preparations from natural foods had suggested the presence of pyridine-like substances and also of hydroxyl groups in a benzene ring, Williams began by synthesizing a series of hydroxy pyridines and other pyridine derivatives. Of these α-hydroxy pyridine, 2-, 4-, 6-trihydroxy and 2-, 3-, 4-trihydroxy pyridine were found to have curative power when tested upon polyneuritic pigeons. "The first of the curative substances tested was α-hydroxy pyridine. Three birds were treated with excellent results. However, three others later showed little or no improvement. On proceeding with the series of polyhydroxy compounds, a rapid striking cure was obtained with a preparation of 2-, 4-, 6-trihydroxy pyridine, followed by several partial or complete failures. A second and third fresh preparation, however, produced two and three rapid cures respectively. . . . In each case all the cures obtained were of those pigeons which were first treated with a given preparation, while those treated with the same preparation a few days or weeks later invariably received no benefit. It was obvious that the substances had changed in some manner so as to lose the curative power. As there was no evidence of decomposition it seemed probable that it was due to isomerization."

This suggested to Williams that an isomerism may be at least partially responsible for the instability of the natural "vitamines" of foods and in conjunction with Seidell he reinvestigated the antineuritic properties of yeast extracts from this standpoint and obtained results indicating that the antineuritic vitamine of yeast is an isomer of adenine.

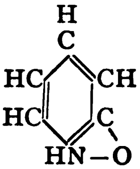
Voegtlin and White report that they were unable to confirm these observations on attempting to repeat the work of Williams and Seidell.

Continuing his work on the relation of chemical structure to antineuritic activity Williams finds that β-hydroxy pyridine, nicotinic acid, trigonelline, and betaine are also capable of existence in forms which are curative in the sense of being "able promptly to dissipate the acute symptoms of polyneuritis gallinarum." "On the basis of these results it may be concluded with reasonable certainty that the relief of the paralysis by such substances is intimately connected with a betaine-like ring."

Williams calls attention * to the fact that, on theoretical grounds, the existence of betaine-like tautomeric modifications of the oxy- and amino-pyrimidines and purines is not less probable than in the case of the corresponding derivatives of pyridine, and proposes to search for active isomers in the pyrimidine series.



Betaine



Probable active form of α-hydroxy pyridine (Williams)

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CHAPTER XIII

FOOD IN RELATION TO GROWTH AND DEVELOPMENT AND THE DIETARY DEFICIENCIES OF SOME INDIVIDUAL ARTICLES OF FOOD

Nutritive Requirements of the Growing Organism

"THE upper limit of the size of an animal is determined by heredity. The stature to which an animal may actually attain, within this definitely fixed limit, is directly related to the way in which it is nourished during its growing period" (Waters).

While feeding experiments upon growing animals and the influence of growth upon food requirements have been discussed to some extent in previous chapters, the great importance of adequate nutrition during the growing period demands special consideration. Recent investigations upon nutrition in growth are also of added interest in that the study of "growth-promoting properties" of food materials has broadened our conceptions of food values and of nutritive requirements in general.

It is a familiar fact that the growing organism needs more energy, protein, and inorganic foodstuffs in proportion to weight than does one which is full-grown. But even a liberal diet made up of purified proteins, fats, carbohydrates, and salts does not suffice to support normal growth and complete development.

Growth-Promoting Substances in Food

Hopkins * found that the addition of very small amounts of milk to diets otherwise composed of purified foodstuffs sufficed

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* As early as 1906, Hopkins had found experimentally and published in brief (*The Analyst*, Vol. 31, page 395) the fact that an animal cannot live "upon a mixture

to induce growth in young rats (Fig. 12), and Osborne and Mendel demonstrated that a similar growth-promoting effect was obtained when they introduced into their rations of isolated foodstuffs a moderate amount of "protein-free milk" — a powder made by removing the fat, the casein, and the albumin from cow's milk and evaporating the clear filtrate to dryness. Since in both these investigations it was found that milk ash does not show this property, it follows that milk must contain some water-soluble organic substance which exerts a distinctly favorable effect upon growth. A little later it was found both by McCollum and Davis and by Osborne and Mendel that the fat of milk (butter fat) also exerts a growth-promoting influence, which, as it is shared by only certain other fats, is probably not due to the glycerides themselves, but rather

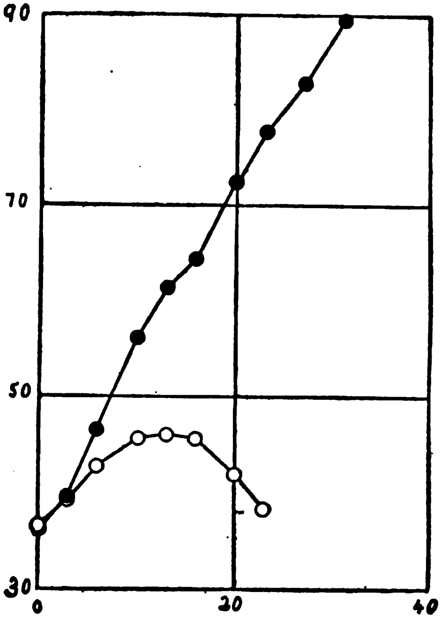

FIG. 12. — Growth curves of rats. Lower curve six rats on artificial diet alone. Upper curve six similar rats receiving in addition 2 cc. of milk each per day. Abscissæ time in days: ordinates average weight in grams. Courtesy of Dr. F. Gowland Hopkins.

of pure protein, fat, and carbohydrate, and even when the necessary inorganic material is carefully supplied the animal still cannot flourish." Seeking further light upon the chemical nature of the essential substance contained in milk and some other natural foods but not in the purified foodstuffs, he deferred publication of the details of the experiments until 1912 (*Journal of Physiology*, Vol. 44, page 425).

to a fat-soluble substance carried by butter-fat and the fat of egg yolk and in much smaller quantities if at all by most vegetable and meat fats. This fat-soluble substance (or something showing the same growth-promoting property) has also been found by McCollum to occur in certain plant tissues not rich in fat, notably in alfalfa and cabbage leaves and presumably in leaves generally. Normal growth and full development, as shown by ability to produce and nourish healthy young, demands, therefore, in addition to adequate and appropriate supplies of proteins, fats, carbohydrates, and salts, at least two substances or kinds of substances which are distinguished by the solubility of one in water and of the other in fat. These substances, neither of which has yet been chemically identified, are variously designated by different writers. Hopkins used the term "accessory factors." Funk calls them "growth vitamines." McCollum criticizes the use of the term "vitamine" and proposes that until chemically identified the substances be known as "fat soluble A" and "water soluble B." The fats of milk, eggs, and certain organs, and also the leaves of certain plants, are particularly rich in "fat soluble A" whereas many staple foods are very poor in this constituent. "Water soluble B" is more widely distributed, being found in the foods which have antineuritic properties, and it probably is the same as the substance whose absence or insufficiency induces polyneuritis.

Thus the feeding experiments with isolated foodstuffs have resulted in establishing the fact (until recently unsuspected and doubtless responsible for many of the failures met in earlier experiments) that there are required for normal nutrition, and most conspicuously during growth and development, these two factors A and B in addition to the previously known factors of ample energy and adequate and appropriate supplies of protein and of inorganic foodstuffs. This has made it possible to proceed much more intelligently and effectively in the study of the relations of ordinary food materials to growth and development. In this connection it is important, as McCollum has emphasized, that growth and development be considered not only in terms of gain in weight at a normal rate, but also in reference to the capacity to produce and nourish healthy young at intervals normal for the species. A diet lacking in growth-promoting properties is apt to have an unfavorable effect upon reproduction and lactation. In some cases a deficiency may become manifest in connection with reproduction, even when it has not appreciably retarded growth.

In a recent summary,* McCollum points out that the deficiency of wheat as a sole food has been found to be associated with the nature of its proteins, of its ash constituents, its lack of the "fat soluble A," and possibly a toxic factor. He states that when wheat and a good salt mixture are fed there is improvement in the condition of the experimental animals for a limited time. A rat will grow for a month † on this combination and then stop, whereas he could not grow at all on wheat alone. On feeding wheat and casein only there is also a marked improvement for a time, and the same is true for a mixture of wheat and butter fat, "but in no case does the beneficial effect extend beyond the first month. These results we interpret to mean that there were two at least of the dietary factors involved, unless the trouble was all the result of toxicity in the wheat kernel. The next step was to feed wheat together with two purified additions as wheat, salts, and casein; wheat, salts, and butter fat . . . combinations (which) will make a young rat grow to practically the normal adult size and at nearly the normal rate, but rats so fed will never produce young, and will never live much beyond a third of the usual length of life of a well-nourished animal. When we feed wheat with all three of the purified additions, salts, protein, and butter fat, the animals are perfectly nourished and not only grow up at the regular rate but they are able to reproduce at frequent intervals and to successfully rear their young, and these young can complete the life cycle with no other food than that on which their parents lived."

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* McCollum. The Present Situation in Nutrition, *Hoard's Dairyman*, July–August, 1916.

† In a month a rat makes as large a fraction of his total growth as is made by a child in from one to two years.

Thus it now appears that the diet in order to be fully and permanently satisfactory must furnish (1) adequate energy value, (2) proteins sufficient in quantity and suitable in their amino acid make-up, (3) ash constituents each in sufficient quantity and all in well-balanced proportions, (4) "fat soluble A," and (5) "water soluble B." All of these factors are doubtless necessary in order to make the diet really adequate at any time, but it is through studies of growth that the last-mentioned factors were found, and all of the requirements are plainly more prominent in connection with growth, development, and reproduction than in the simple maintenance of healthy adults.

Recognition of some of the factors just mentioned is too recent to have influenced the arrangement of many of the feeding experiments which have been made for the purpose of studying the relation of diet to growth, so that it is not always possible to interpret the experimental data in terms of these five categories. This can, however, be done to some extent.

Influence of Restricted Food Supply

(1) ENERGY

When a diet of such character as would ordinarily meet all requirements is fed to a growing animal in amounts too small to meet the growth requirement, it is plain that such restriction may result in a deficiency of one, several, or all of the essential factors. If the diet is so selected as to be relatively rich in proteins, ash constituents, and the factors A and B, then restriction of the amount of food will result primarily in an *energy* *deficit.* Waters has described experiments which appear to have been of this character. He reports numerous cases of young cattle kept on restricted amounts of food of suitable kinds, the restriction being such as to materially retard the increase in weight as compared with that of a full fed animal of the same age, or even to hold the young animal at stationary weight at an age when it should have been growing rapidly. In such cases of insufficiency of the total food (energy) intake the skeleton continues to grow, in height at least, while adipose tissue steadily disappears, and the muscles become more or less depleted. In a young animal subjected to this type of under-nourishment the skeleton grows in height to a much greater extent than in width. Thus in a full-fed steer the increase in length of foreleg and in width of chest were about equal, while in one whose rate of growth was retarded by sparse rations the width of chest increased only one third as much as the length of foreleg, and in another animal of the same age whose food was so restricted as to permit no increase in weight the increase of chest-width was only one eighth as much as the increase in foreleg. The ratios actually measured in typical cases were as follows:

CONDITION OF ANIMAL	WIDTH OF CHEST	:	LENGTH OF FORELEG
I — full fed	1	:	0.97
II — retarded	1	:	3.13
III — maintenance *	1	:	8.00

Along with the narrower skeleton the underfeeding resulted in muscles of smaller diameter, absence of subcutaneous fat, and a general emaciated appearance. Young animals thus held at constant weight when they should be growing are in reality undergoing starvation. To quote from Waters' paper:

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* Just enough food to maintain constant weight in an animal which should have been growing rapidly had he been more liberally fed.

"Apparently the animal organism is capable of drawing upon its reserve for the purpose of sustaining the growth process for a considerable time and to a considerable extent. Our experiments indicate that after the reserve is drawn upon to a certain extent to support growth, the process ceases and there is no further increase in height or in length of bone. From this point on, the animal's chief business seems to be to sustain life. This law applies to animals on a stationary live weight as well as those being fed so that the live weight is steadily declining, and indeed to those whose ration, while above maintenance, and causing a gain in live weight, is less than the normal growth rate of the individual. Such an animal will, while gaining in weight, get thinner, because it is drawing upon its reserve to supplement the ration in its effort to grow at a normal rate."

"On all the animals under observation the retardation in height growth did not manifest itself at all until after the sparse nourishment had been continued for several months. On the other hand, the influence upon the width development was observable much earlier, and width development ceased altogether, in the case of animals on a maintenance or submaintenance ration, long before the height development had ceased."

"Our experiments have shown that within certain limits which are not yet at all well defined, retarded growth means retarded development of the organism. Thus an animal at twelve months of age and weighing on account of sparse nourishment only 400 pounds when it should under natural nourishment have weighed 800 pounds, has not its tissues as fully developed and matured as they would have been had the nourishment been normal. For example, we find that the flesh of steers 14–16 months old that had been sparsely fed throughout their lives presented the general characteristics such as color, flavor, etc. of veal or the flesh of calf. At this age the flesh of a highly nourished animal possessed the characteristic color, texture, and flavor of beef. Prof. Eckles has shown that dairy heifer calves heavily fed reach sexual maturity at from eight to ten months of age, whereas similarly bred individuals that were sparsely fed did not reach the stage of puberty under from 16 to 19 months of age."

" An animal which has been retarded and which in its earlier life has shown an asymmetric development, may tend later to correct this asymmetry, and it is not inconceivable that this may be fully corrected before the animal has reached a state of complete maturity, or a point where growth ceases altogether."

Somewhat similar experiments have been performed upon dogs by Aron. Here also when the food was suitable in character but too limited in amount to support normal growth the young animals grew in length and height but became thinner. Because of the " growth impulse " such an underfed young animal burns his reserve of body material to cover the deficit in the energy intake " in his endeavor to grow at a normal rate." Such a condition continued indefinitely results after a time in cessation of all growth and finally in death from starvation. A dog which by underfeeding had been kept for a year at the weight which he had when 5 weeks old and had become long, tall, and very thin, and was then fed liberally immediately gained in weight and circumference but appeared to have lost the capacity for further growth in length and height. If, however, the period of underfeeding be not too prolonged, the animal on subsequently receiving ample food may regain normal proportions and grow to full normal size.

Since stationary weight in the young animal which is attempting to grow with an insufficient energy supply does not mean cessation of all growth but growth of bone and brain at expense of adipose tissue and to some extent also of muscle, it follows that the body of such an animal gradually changes in composition, the percentages of fat and perhaps protein becoming less while the percentages of water and ash increase. If, however, the diet is rich in fat, as in experiments upon mice recently reported by Mendel and Judson, a simple diminution of the amount of food to a point where gain in weight ceases may not result in any such general replacement of fat by water, perhaps because in such a case the stunting may be due to insufficiency of some of the other factors rather than to an energy deficit.

The experiments of Mendel and Judson also yield interesting data regarding the changes which normally occur in the water, fat (ether extract), and ash content of the body during its most active growth. From 88 analyses of the entire bodies of mice the following changes in composition were found: (a) increase in solids from 16 per cent at birth to a maximum of 35 per cent at fifty days with a subsequent decrease to 33 per cent; (b) decrease in the proportion of water in the fat-free substance from 85.5 per cent at birth to 73 per cent in the adult mouse; (c) rapid increase in fat from 1.85 per cent at birth to about 10 per cent followed by slow increase to 12 per cent; (d) increase in ash content from 1.86 per cent at birth to 3 per cent in the adult mouse.

(2) PROTEIN

As explained in earlier chapters (text and figures, pages 55–68 and 224–226), it was shown by Osborne and Mendel that with a diet adequate in all other respects any one of a number of purified proteins such as casein, lactalbumin, or edestin might serve as the sole protein both for maintenance and for growth, while gliadin as sole protein food sufficed for maintenance but not for growth, and zein as sole protein did not suffice even for maintenance. Gliadin contains adequate tryptophane but only about 1 per cent of lysine; addition of lysine to the gliadin ration made it adequate for growth. Zein contains neither tryptophane nor lysine; addition of tryptophane to the zein diet makes it adequate for maintenance; addition of both tryptophane and lysine makes it adequate for growth.

When "adequate" proteins were fed in progressively restricted amounts, *i.e.* in diminishing percentage of the food mixture, Osborne and Mendel found that with different proteins different amino acids prove to be the limiting factors — *e.g.* lysine in the case of edestin, cystine in the case of casein. With 15 to 18 per cent of casein in the food mixture the rate of growth was normal; with 9 to 12 per cent of casein the rats grew more slowly but normal rate of growth was resumed upon adding 3 per cent of cystine to the food mixture. With only 4.5–6 per cent of casein the addition of the 3 per cent cystine did not make the growth normal, indicating that with casein reduced to this point the supply of some other amino acid had become insufficient.*

Another case in which cystine appears to have been a determining factor in tissue growth has been recorded by Evvard, Dox, and Guernsey in connection with their feeding experiments upon pregnant swine. Here a difference in the hair coats of the new-born pigs appeared to be due to the different intake of cystine in the food protein consumed by the mother, hair being rich in sulphur, and cystine the sulphur-bearing amino acid of the food.

A so-called incomplete protein, *i.e.* one which when fed alone is quite inadequate to meet the requirements of protein metabolism, may nevertheless contribute toward these requirements to an important degree and may even play a prominent part in promoting growth, as was strikingly demonstrated by Osborne and Mendel in experiments in which they added zein to a ration containing a small percentage of lactalbumin. (See Fig. 4, page 66.) Here the addition of zein to the ration more than doubled the rate of growth. Still more recently McCollum, Simmonds, and Pitz, feeding rats on rations composed of a single grain with supplementary additions, find that gelatin supplements wheat proteins excellently though it apparently does not appreciably improve the proteins of maize or oats. Since gelatin, although lacking tyrosine and tryptophane is relatively rich in lysine, these results are interpreted as indicating that lysine is probably the limiting factor in wheat proteins but not in the proteins of the maize or of the oat kernel.

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* *Journal of Biological Chemistry*, Vol. 20, page 351.

In view of such evidence it is important to guard against the erroneous impression that incomplete proteins are useless for growth. The illustrations just given show that the growing organism may use such proteins to extremely good advantage; but the " incomplete " proteins must not be permitted to displace the " complete " proteins to too great an extent if the young organism is to grow and develop at a fully normal rate.

When growth is retarded by inadequate intake of protein or of a particular amino acid, the emaciated appearance characteristic of animals attempting to grow on an insufficient energy intake is not to be expected. Osborne and Mendel have recorded numerous cases of suspension of growth of young rats, especially when kept on rations containing gliadin as a sole protein food. Here the inadequacy of the lysine intake results in retardation or even complete suspension of growth, but the animal may remain quite healthy and symmetrical. Moreover rats may be subjected to this type of stunting for a remarkably long time (even as long as would normally cover the entire growth period) and still retain their capacity to grow when given an adequate diet.

In some cases * " after periods of suppression of growth, even without loss of body weight, growth may proceed at an exaggerated rate for a considerable period. This is regarded as something apart from the rapid gains of weight in the repair or recuperation of tissue actually lost. Despite failure to grow for some time the average normal size may thus be regained before the usual period of growth is ended." Statistical studies

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* Osborne, Mendel, Ferry, and Wakeman. *American Journal of Physiology*, Vol. 40, pages 16–20 (1916).

on children also indicate that retardation in early growth can usually be made up by extra rapid growth later.*

Mendel and Judson have studied the influence of different types of protein stunting upon the composition of the body in the case of the mouse. They find that when abundance of fat is furnished in the diet, but not enough protein to maintain normal growth, the percentage of fat in the animal becomes greater than when the food contains an adequate amount of protein with the same proportion of fat. They suggest that: "There seems to be a tendency to protect the limited amount of protein by increasing the available supply of fat in the body." "This does not occur when growth is arrested by lack of lysine, as in the use of gliadin as the only protein in the diet, since in this case the limiting factor lies not in the amount but in the nature of the protein."

(3) ASH CONSTITUENTS

Ash constituents have long been recognized as playing an important part in the growth of young animals and of these, as we have already seen, the elements most likely to be deficient are calcium, phosphorus, and iron. Infants (and young mammals generally) are born with a reserve store of iron usually sufficient to supply the growth requirement up to about the end of the normal suckling period. At any time after this initial reserve supply has been used, the iron in the body will be found very largely localized in the blood. The blood constitutes less than 7 per cent of the weight of the body but contains more than 70 per cent of its iron content. Hence a deficit of iron becomes more noticeable in the blood than in the other tissues — growth may not cease but the child (or young animal) may grow anemic; experiments illustrating this have been cited in the chapter on iron, and it has been shown that inorganic forms of iron are not of equal nutritive value with the organic forms which occur naturally in food materials. To an even greater extent than the iron is localized in the blood, the calcium of the body is localized in the bones; it is estimated that the bones contain over 99 per cent of the body calcium. An inadequate supply of calcium in the food during growth retards the development and calcification of the bones. The calcium needed by the growing organism can be assimilated from inorganic forms. Both of these facts are illustrated by the experiment of raising puppies on meat with and without bones to gnaw as described in Chapter XI. It has also been found that the addition of calcium chloride and calcium carbonate to a basal ration of corn and common salt in the case of pregnant swine resulted in greater size, more vigor, bigger bone, and better general condition of the new-born pigs (Evvard, Dox, and Guernsey).

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* Mendel. *Biochemical Bulletin*, Vol. 3, page 167.

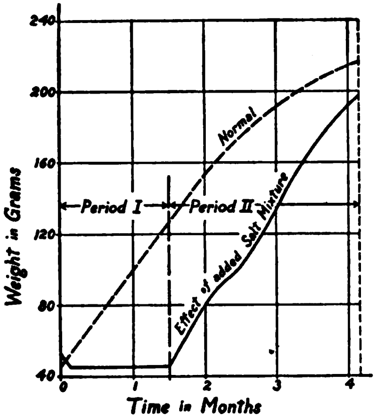

FIG. 13. — Effect upon growth of adding to a diet otherwise adequate a salt mixture of such composition as to make the composition of the total ash similar to that of milk ash; immediate resumption after entire suspension of growth. Courtesy of Dr. E. V. McCollum.

Bone development may also be interfered with by inadequacy of the phosphorus supply. Several investigators, in studying the effect of diet upon growth of bone, have found that the bones formed in a young animal kept on phosphorus poor diet are apt to be soft, spongy, and weak (of low breaking strength), and that this may be prevented by the simple addition of calcium phosphate to the food.

Since phosphorus is a prominent constituent not only of bones but of all the soft tissues as well, the effects of a phosphorus deficiency may be far-reaching. In the experiments of Hart, McCollum, and Fuller, young pigs on phosphorus-poor food continued to grow for some time but finally developed not only the bone defects just noted but also weakness of the legs, stupor, and a more or less comatose condition accompanied by twitching of the muscles, dragging of the hind quarters, and ultimately loss of weight and collapse. These effects were all prevented by simple addition of calcium phosphate to the food.

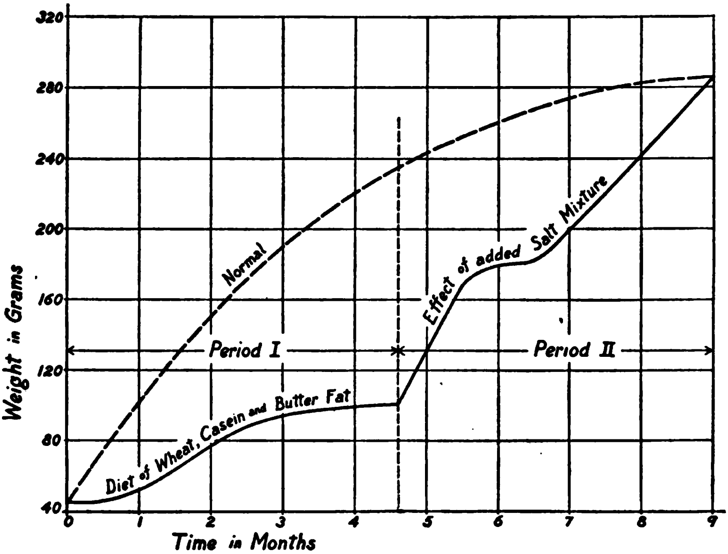

FIG. 14. — Growth at much less than half the normal rate through the greater part of the normal growth period, followed by accelerated growth upon adding a suitable salt mixture to the diet. Courtesy of Dr. E. V. McCollum.

Hart and McCollum record cases in which swine restricted to a ration of corn meal and corn gluten showed little or no growth, but began to make good growth upon addition to the food of such salts as to make the ash content of the ration similar to that of milk.

McCollum, Simmonds, and Pitz have likewise shown that a defective inorganic content of the diet may also result in retardation or suspension of the general growth of the young animal, which may be followed by prompt resumption of growth (even at an accelerated rate so that the normal weight for the age may be regained) when a salt mixture is added such as to make the total ash of the ration similar in composition to milk ash (Figs. 13 and 14).

(4) Vitamines or Food Hormones

Osborne and Mendel (1913) found that the use of highly purified salts in rations of isolated food substances resulted in less growth than when salts of only ordinary purity were fed. This suggested to them that other inorganic salts might be needed, and a ration containing very small additions of salts of iodine, fluorine, manganese, and aluminum was fed with somewhat more favorable results than had attended the use of the usual (simpler) salt mixture; but none of their diets composed entirely of pure substances gave as good results as the corresponding food mixtures in which "protein-free milk" was used, and they concluded that the latter was unquestionably superior to any purely artificial food mixture. This superiority now seems to be attributable primarily to the presence in the "protein-free milk" of the "water soluble B," probably identical with the antineuritic "vitamine." If the latter is the case, the substance is not confined to milk but is fairly widely distributed among natural food materials. Less widely distributed is the other "essential accessory" furnished by milk,

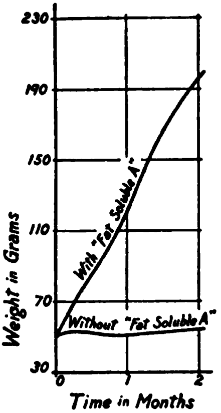

Fig. 15. — Effect upon growth of adding "fat soluble A" to a diet adequate in all other respects. Courtesy of Dr. E. V. McCollum.

the so-called " fat soluble A," to the presence of which in butter * is attributed its marked growth-promoting property as shown independently by McCollum and Davis and by Osborne and Mendel. The latter find that in a diet containing "protein-free milk" and an adequate protein, 5 per cent of butter fat usually suffices to insure normal growth and in a few cases from 1 to 3 per cent has seemed sufficient. When butter fat is fractionally crystallized from alcohol the growth-promoting factor remains in the oil fraction, the fractions of higher melting point being ineffective. Lard and olive oil were also found ineffective, while cod liver oil resembled butter fat in its growth-promoting property, and beef fat shows the same property to a less degree. McCollum finds the same property in the fat of egg yolk and of animal organs such as the kidney, but in no commercial fat of vegetable origin thus far examined, although feeding experiments with whole grains and grain embryos indicate that their fats must carry appreciable amounts of this growth-promoting substance. He finds also, as noted earlier in the chapter, that the same " fat soluble A " (as demonstrated by

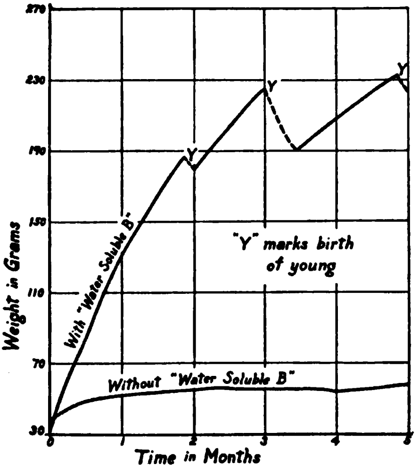

FIG. 16. — Effect upon growth of adding "water soluble B" to an otherwise adequate diet. Courtesy of Dr. E. V. McCollum.

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* According to McCollum, "fat soluble A" is about 30 times more soluble in fat than in water. In milk about half of it is dissolved in the small volume of fat and about half in the large volume of water present. Skimmed milk is, therefore, not wholly devoid of this substance.

specially arranged feeding experiments) occurs in relative abundance in alfalfa and cabbage leaves and probably in green vegetables and forage plants generally. The accompanying charts (Figs. 15 and 16) show the effects of presence or absence of A or B upon the growth curves of young rats. Recognition of the independent need for each of these substances or groups of substances is too recent for definite correlation of each with a distinct type of stunting. Both "fat soluble A" and "water soluble B" are held to be essential for the maintenance of health as well as for growth. The fat soluble A appears to be dispensable, when maintenance alone is involved, for a somewhat longer period than is the water soluble B, which accounts for the polyneuritic symptoms in birds kept on polished rice diet and the cure of these symptoms by the feeding of extracts of foods rich in the water soluble B. Thus McCollum and Kennedy find "that pigeons can be brought into the polyneuritic state by feeding a diet free from both the essential factors A and B, and can be completely cured and maintained in a normal condition for at least 35 days on the same diet which brought on the disease, plus the water extract of a foodstuff (rolled oats) on which rats cannot grow without the addition of butter fat, but on which they do grow when the latter is added."

Dietary Deficiencies of Individual Articles of Food

McCollum and his associates are now applying the above conceptions to the study of the dietary deficiencies of individual articles of food. In a recent paper * they present their plan of investigation as follows:

"If a single natural food product fails to nourish an animal adequately, it may be due to: (*a*) lack of sufficient protein, or to proteins of poor quality; (*b*) an unsatisfactory mineral content due either to inadequacy of certain elements in amount, or to unsatisfactory proportions among them; (*c*) an inadequate supply of the fat soluble A; (*d*) of the water soluble B; (*e*) or some toxic substance contained therein. One, two, three, four, or all of these factors may operate in inducing nutritive disturbances.

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* McCollum, Simmonds, and Pitz. *Journal of Biological Chemistry*, Vol. 25, pages 105, 132 (May, 1916).

" It should be obvious that a systematic procedure in which we feed the substance under investigation supplemented with (*a*) pure protein only, (*b*) salt mixture additions only, (*c*) butter fat only, (*d*) extracts known to carry the water soluble B and as little else as is possible, will reveal whether the failure of nutrition involves one factor only, or more than one. If more than one factor is involved, a similar procedure, but with the addition of all possible combinations of pairs of the isolated food ingredients listed above, followed if need be by another series of feeding experiments in which animals are fed the natural foodstuff supplemented with three such uncomplicated additions, in all possible combinations, and if necessary another experiment in which all four additions are made, will give us results which make it possible to consider the components of our rations in an entirely new light. Provided the foodstuffs contain a toxic substance, special procedures will have to be devised for studying its effects.

" Similar studies must also be made by this method of procedure, with pairs of the important foodstuffs (food materials) in varying proportions, the variation of the mixture including sufficient range to reveal the degree to which the deficiencies of the protein mixture of one grain are corrected by the peculiar quantitative relationships among the amino acids yielded by the proteins of the other grain. The same may be said for the factors other than protein. In this way we shall become able to interpret the biological value of the mixtures of natural foodstuffs which make up the rations which are in common use, in which the attempt is now made to make for safety through variety. We have carried our inquiry into the nature of the dietary deficiencies of several natural products far enough to convince us of the practicability of this method of study."

Following this general plan McCollum and his associates have studied the dietary deficiencies of wheat, wheat embryo, rice, maize, oats, and beans. While some of the results thus obtained have already been cited, it may be well to summarize here the chief findings with reference to each of these food materials in succession. In all cases the experiments were chiefly upon rats.

The wheat kernel when fed alone did not induce normal growth in the experimental animals. Addition of either (1) purified casein, (2) butter fat, or (3) a suitable salt mixture such as to make the total ash of the ration resemble milk ash in composition, was found to improve conditions to some degree in each case, but in no case did such a single addition result in normal growth. Neither could fully satisfactory results be secured by the addition to the wheat ration of any two of these three factors mentioned; but when all three were added, the animals showed complete growth and normal reproduction. Hence McCollum concludes that the wheat kernel is deficient as a food (1) in the poor quality of its protein, (2) in that it furnishes an inadequate supply of " fat soluble A," (3) in that it has an unsatisfactory inorganic content. He also believes that when the diet is chiefly made up of the entire wheat kernel, including embryo, the possibility of a mild toxicity, due to a toxic constituent in the embryo, must also be reckoned with.

Wheat embryo when fed alone did not induce growth although it is rich in proteins of high nutritive efficiency and in water soluble B, and not deficient in fat soluble A. It is deficient in its inorganic content; even so simple a modification as the addition of 2 per cent of calcium lactate to the wheat embryo diet may induce noteworthy growth where otherwise no growth takes place. To an important extent, according to these authors, the failure of rats and swine to grow on diets consisting largely of wheat embryo is attributable to a toxic substance contained therein, which appears to be associated with the fat. Extraction of the fat by ether removes in great measure the toxicity of the embryo without necessarily making the food deficient in the fat soluble A. According to the authors the toxicity may be overcome by the simple addition of casein to the diet. That diet may greatly influence susceptibility to toxicity was reported by Hunt in 1910. Hunt found great differences in susceptibility to acetonitrile poisoning, which differences appeared to be due to diet alone.*

Polished rice as a diet for growth was found to be deficient in four respects: (1) its protein content seemed too low for maximum growth; (2) it contained inorganic elements in insufficient amounts and also not in proper proportions; (3) it was found deficient in fat soluble A; (4) it lacked water soluble B.

Maize when fed alone induced no appreciable growth, nor could a suitable diet be made by mixing the parts of the maize kernel in different proportions. The proteins of the maize kernel contain all the amino acids essential for growth, but it is held that the proportion of certain of them is such that when this is the sole source of protein the growth is never more than about two thirds normal. The maize diet always requires the addition of a suitable salt mixture (or food of suitable ash content). Also the amount of fat soluble A is insufficient in maize to induce growth at the normal rate. Normal growth and reproduction, however, occurred when maize was supplemented by butter fat, purified casein, and a suitable salt mixture.

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* "In extreme cases mice after having been fed upon certain diets may recover from forty times the dose of acetonitrile fatal to mice kept upon other diets. It is, moreover, possible to alter the resistance of these animals at will and to overcome the effects of one diet by combining it with another. . . . The experiments with oats and oatmeal and eggs are of especial interest. In the earlier parts of this paper many experiments were quoted showing that a diet of oatmeal or of oats usually leads to a marked resistance of mice to acetonitrile; the experiments quoted in this section which show that the administration of certain iodine compounds with or subsequently to such a diet further increases this resistance, and the experiments previously reported showing that as far as the resistance toward acetonitrile is concerned iodine exerts its action through the thyroid gland, all point to the conclusion that the resistance caused by an oat diet is in part an effect exerted upon the thyroid. This effect is obtained much more markedly and constantly with young, growing mice. From these experiments and considerations it seems very probable that it is possible to influence, in a specific manner, by diet, one of the most important hormones in the body; this is a comparatively new principle in dietetics and one which may prove of much importance" (Hunt, *The Effect of a Restricted Diet and of Various Diets upon the Resistance of Animals to Certain Poisons*, pages 56, 73).

The oat kernel, according to McCollum's investigations, contains protein of poorer quality than either the maize or wheat kernel. When all other dietary factors are properly adjusted, nine per cent of oat protein in the diet serves to induce slow growth for a time, but never for more than about a month (experiments with rats). Casein, which serves as such an efficient adjunct to the wheat and maize proteins, does not seem to supplement oat protein in a very satisfactory manner; a diet with 9 per cent of protein from the oat kernel and 10 per cent purified casein did not induce growth at a maximum rate as did similar combinations of casein with wheat and maize proteins. In this connection McCollum reports the unexpected finding that gelatin supplements the protein of the oat kernel more effectively than does casein.

The ash constituents of the oat kernel must always be supplemented in order to induce growth. Fat soluble A is present in the oat kernel in very small amounts. The amount of water soluble B is adequate. Growth at more than half the normal rate may be obtained when the oat diet is supplemented by the addition of a suitable salt mixture and either butter fat or a suitable protein. When all three of these supplements are added, growth is normal but somewhat slow. McCollum believes that excessive feeding of the oat kernel causes some injury to the animal.

The white bean, when fed as the chief component of the diet, gave results indicating that its proteins are of lower nutritive efficiency than those of the cereal grains. The bean protein can be supplemented by the addition of 9 per cent of casein to the diet. The inorganic content of the white bean is not such as to induce growth, but must be supplemented by a suitable salt mixture (or by food of a different ash content from that of the bean alone). The white bean seems to contain less of fat soluble A than do the cereal grains. It contains water soluble B in abundance. The bean diet appeared to exert an unfavorable effect in that animals fed on a diet containing a smaller proportion of beans (25 per cent of the total food) seemed better nourished than those whose diet contained a larger proportion. It is suggested that beans may contain some unknown substance which is harmful when taken in too large an amount; or that the pressure of the intestinal gases resulting from fermentation of the hemicelluloses for which the higher animals have no digestive enzyme may result in a somewhat asphyxial condition of the intestinal wall, thus interfering with the normal processes of absorption and unfavorably affecting the general condition of nutrition.

Seeds in general are held by McCollum to require supplementing in order to make a diet which will support normal growth and reproduction. As supplement to a diet consisting largely of the products of cereal grains or other seeds, milk is found to be especially effective. It is also found that while seeds are not effectively supplemented by other seeds, they may be supplemented by the leaves and probably also by the roots and tubers of plants so that it is feasible, if desired, to draw a balanced diet, adequate for all the requirements of growth and reproduction in an omnivorous animal, entirely from the products of plants. Thus McCollum kept rats through four generations upon a carefully adjusted ration of maize, alfalfa, and cooked peas. Growth and reproduction were normal. The mothers successfully suckled young up to the normal age of weaning, after which they took the same food mixture as the adults. In this connection it is interesting to note that rats which were free to make their own selection from a much greater variety of vegetable foods never grew beyond half the normal adult size.

In practice milk is found to be most highly efficient as a supplement to diets consisting largely of seeds or their products: "The dietary should be built around bread and milk." The chemical constitution of its proteins and its high calcium and vitamine contents are all factors in the unique nutritive efficiency of milk, and make it possible for a moderate addition of milk to render adequate a diet otherwise composed entirely of seeds.

Cotton-seed meal or flour * constitutes an abundant and concentrated source of protein and energy which as yet has been but little utilized in human nutrition. This is doubtless largely because bad results have sometimes followed its use in stock feeding, leading to the general belief that it is somewhat toxic, at least when used in considerable quantities. Withers and Carruth succeeded in extracting from the kernels of the cotton-seed a substance, *gossypol*, which shows deleterious action when fed and to which the toxicity of raw cotton seed and of some cotton-seed meals was attributed. This substance, however, is thermo-labile, and apparently is more or less completely destroyed by the heating to which cotton-seed meal or flour is ordinarily subjected in connection with the processes of crushing and pressing. Feeding experiments to determine whether the well-prepared cotton-seed meal or flour now available for human food has any appreciable toxicity, and to what extent it meets the nutritive requirements of normal growth and reproduction, have recently been reported by Richardson and Green and by Osborne and Mendel. Richardson and Green, feeding a high-grade commercial cotton-seed flour, found that no evidence of toxicity appeared although this flour constituted

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* Cotton-seed flour is prepared by finely grinding, sifting, and perhaps also aspirating the meal so that particles of lint, hulls, etc., are removed more completely than from the ordinary cotton-seed meal used in stock feeding.

45 to 50 per cent of the ration of albino rats through four successive generations or during 565 days of the life of an individual (about two thirds the entire normal life span); that the cotton-seed flour met all protein requirements of maintenance and growth, and when supplemented with protein-free milk and butter fat was able to support normal growth and reproduction. They found that no better growth was induced, but more frequent reproduction with lower mortality and more general well-being of animals were obtained when 5 per cent of casein was added to a diet containing 50 per cent cotton-seed flour with butter fat, protein-free milk, lard, and starch. Normal growth and reproduction did not result from diets containing 50 per cent cotton-seed flour in which there was a lack of butter fat, protein-free milk, or both. On a diet containing fifty per cent cotton-seed flour with the addition of casein and butter fat, but with no mineral matter other than that from the cotton seed, rats grew normally and reproduced, but the second generation did not make quite normal growth.

Osborne and Mendel also found the proteins of cotton-seed flour to be efficient in nutrition, not only when fed alone in relatively abundant amounts but also when used as supplements to maize protein. They obtained toxic effects from the feeding of cotton-seed kernels but not from the cotton-seed flour. Like Withers and Carruth they demonstrated that the harmful substance could be removed from the kernels by extraction with ether; but the kernels can also be rendered harmless by steaming, which is a step in the usual commercial process of extracting the oil. The results of heating were, however, not altogether uniform and Osborne and Mendel suggest that undue heating may render the meal unpalatable or otherwise unsuitable for nutrition, in addition to destroying the original deleterious substance, and that these facts may help to explain the conflicting evidence regarding the alleged suitability of different samples of commercial meals.

These recent investigations upon cotton-seed flour are worthy of careful study both because of the great economic importance of this material and because they illustrate well the application of modern methods of nutrition research to the solution of a long-standing problem regarding the utility of an abundant but relatively neglected food material.

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CHAPTER XIV

DIETARY STANDARDS AND THE ECONOMIC USE OF FOOD

The General Problem of a Dietary Standard

IT is sometimes asked whether a normal appetite does not indicate, as well as can any dietary standard, the amount of food which is desirable for an individual in any given circumstances.

In considering such a question we shall hardly expect the phrase " amount of food " to indicate equally the energy value, the protein content, the content of each of the necessary chemical elements, and each of the unidentified dietary essentials A and B (or fat soluble and water soluble " vitamines "). Since different articles of food vary greatly in the relative amounts of the various nutrients which they contain, some one aspect of food value must be chosen as a basis in order to give definite meaning to the phrase "amount of food." Inasmuch as the most prominent of the nutritive requirements is the need for energy, and the yielding of energy is the one function in which practically all articles of food take part, it is logical to expect that " amount of food " will more nearly express number of calories than any other one factor of food value or nutritive requirement. Observation confirms this impression and shows that men or other animals when eating varied food under the unrestricted guidance of hunger and appetite tend to take such quantities as are proportioned to the energy requirement whether or not this amount meets also the requirements as to each of the sixteen chemical elements known to be necessary in nutrition.

If then hunger and appetite be regarded as guides, primarily, to the eating of the right amount of food to meet the energy requirement, we may determine their adequacy in any given case by the fatness of the person concerned, since excess of fuel food of whatever kind can contribute to the storage of body fat.

If from year to year the body keeps in good condition for its work and maintains a fairly constant weight which bears such a proportion to the height as to show that a proper amount of fat is being carried, it is reasonably certain that the amount (fuel value) of food eaten in the course of the year is substantially that which is suited to the degree of activity maintained. If, however, by following the appetite, one becomes unduly stout or unduly thin, or does not get sufficient fuel for the energy required for the day's work, or is annoyed by digestive disturbances indicative of improper feeding, it is certain that the appetite is in this case not a perfect standard. Still more often will the individual appetite prove an inadequate guide to such a quantitative combination of the different types of food as shall lead to a well-balanced intake of each of the many essential food constituents. Here the customs and traditions which govern the food economics of the household and which undoubtedly to some extent reflect the accumulated experience of the race serve an extremely important purpose in checking the caprices of the palate and guiding the individual into food habits which are more likely to conform to actual needs than are the dictates of the individual appetite. But the fullest appreciation of the value of household and social traditions in the formation of good dietary habits does not justify the conclusion that such traditions will always lead to the best results, either physiologically or economically. Even if these traditions represented the experience of past generations to demonstrated that muscular work need not increase protein metabolism, if a sufficient amount of fuel be provided in the form of carbohydrates and fats. Hence, when, in providing for muscular work, he proposes to increase the protein in practically the same ratio as the calories, the idea evidently is not that such an increase is necessary, but simply that it was considered advisable on general grounds not to alter very greatly the nature of the diet in increasing its amount.

LANGWORTHY'S COMPILATION OF RESULTS OF DIETARY STUDIES

Occupation of Head of Family	Food per Man* per Day	
	Protein, Grams	Fuel value, Calories
United States:		
Man at very hard work (average 19 studies)	177	6000
Farmers, mechanics, etc. (average 162 studies)	100	3425
Business men, students, etc. (average 51 studies)	106	3285
Inmates of institutions, little or no muscular work (average of 49 studies)	86	2600
Very poor people, usually out of work (average of 15 studies)	69	2100
Canada: Factory hands (average 13 studies)	108	3480
England: Workingmen	89	2685
Scotland: Workingmen	108	3228
Ireland: Workingmen	98	3107
Germany: Workingmen	134	3061
Professional men	111	2511
France: Men at light work	110	2750
Japan: Laborers	118	4415
Professional and business men	87	2190
China: Laborers	91	3400
Egypt: Native laborers	112	2825
Congo: Native laborers	108	2812

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*In calculating these results it is assumed that women consume 0.8 as much food as men, and children of different ages from 0.3 to 0.8 as much as the man of the family.

In explanation of the liberality of his standards Atwater suggested that " the standard must vary not only with the conditions of activity and environment, but also with the nutritive plane at which the body is to be maintained. A man may live and work and maintain bodily equilibrium on either a higher or a lower nitrogen level, or energy level. One essential question is, What level is most advantageous? The answer to this must be sought, not simply in metabolism experiments and dietary studies, but also in broader observations regarding bodily and mental efficiency and general health, strength, and welfare."

Langworthy, maintaining a similar point of view, has collected the data of large numbers of dietaries believed to be fairly representative of the food habits of people of different occupations in the United States and other countries, and stated them in terms of protein and calories per man per day with the results shown on the preceding page.

Langworthy concludes that the results obtained, the world over, for persons of moderate activity, " do not differ very markedly from a general average of 100 grams of protein and 3000 Calories of energy, and that it is fair to say that, although foods may differ very decidedly, the nutritive value of the diet in different regions and under different circumstances is very much the same for a like amount of muscular work." He also points out that in some cases this may not be apparent until allowance is made for differences in body weight. Thus he estimates the average weight of the Japanese professional and business men at 105 pounds, so that their food consumption of 87 grams protein and 2190 Calories corresponds to 105 grams protein and 3120 Calories for a man of 150 pounds, which agrees well with the American average for similar employment.

As a standard for men with more muscular activity, such as mechanics at moderately active work, Langworthy suggests 3500 Calories including 105 grams of protein.

Chittenden differs from those whose standards have been quoted in giving almost no weight to the results of dietary studies, holding that these serve chiefly as a measure of self-indulgence, and that the true measure of what the body will most profitably use is to be found in the results of experiments upon the protein metabolism, such as have been described in Chapter VIII. On the basis of these experiments he proposes as a standard allowance for the man of 70 kilograms body weight, 60 grams of protein and 2800 Calories per day. For business and professional men such as Chittenden evidently has in mind, the allowance of 2800 Calories is in substantial agreement with earlier estimates. Sixty grams of protein for a man of 70 kilograms is, however, decidedly lower than any standard previously current.

Energy Allowances for Adults

It has been shown in a previous chapter that different normal individuals of similar age and physique are substantially alike in their energy requirement when performing equivalent amounts of muscular work, and that it is primarily the muscular activity, and not personal idiosyncrasy or the amount of food eaten, which determines the amount of energy transformed in the body. A dietary standard of high fuel value, and designed to maintain metabolism on a high energy level, provides, therefore, primarily for a large amount of muscular work. If this work is not performed and the food continues to be eaten and digested, we may expect to find a storage of fuel in the body chiefly in the form of fat, and this is true whether the surplus food eaten is carbohydrate, fat, or protein. Thus the store of body fat which a person carries is the most reliable indication as to whether the amount of food habitually eaten is or is not properly adjusted to the work performed. The storage of fat does, however, in itself modify the food requirement. While it is true, as has been shown, that, as between a lean and a fat man having the same weight, the lean man will have the greater food requirement, yet it is also true that when any given man becomes fat, his increased size of body calls for increased metabolism of energy. The work involved in walking, for example, will increase in proportion to the weight moved (*i.e.* to the weight of the body as a whole); and the work of respiration will increase about in proportion to the weight of that part of the body which must be moved with the expansion and contraction of the lungs; while, if fat is deposited in such a way as to interfere directly with the free play of the muscles, there may be an actual lowering of muscular efficiency, so that a larger expenditure of energy may be required in order to produce a given amount of work. If the liberal diet is continued and the digestion remains normal, the storage of fat will continue until it raises the energy expenditure of the body to a point where the food is no longer in excess. If the store of fat carried when this point is reached is excessive, the fuel value has been too high; if the store of fat is not excessive, the fuel value of the diet, although greater than would have been necessary to maintain the body at its former weight, has not been too high, and the body has acquired an asset whose utility may not always be recognized in health, but which may be of great value in case of accident, illness, or exposure.

Opinions differ somewhat as to the desirable degree of fatness as indicated by the relation of height to body weight.

Hill * estimates the average height at 25 years of age as 5 feet 3 inches for women and 5 feet 8 inches for men, and the corresponding average weights as 119 and 150 pounds respectively. He considers that variations of 10 to 15 per cent above or below the average should be considered normal. According to this estimate the woman of 5 feet 3 inches should weigh not less than 102–107, nor more than 131–136 pounds, and the man of 5 feet 8 inches not less than 128–135, nor more than

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* *Recent Advances in Physiology and Biochemistry.*

165–173 pounds. These figures are exclusive of clothing. Hill considers as "fat" those persons whose weight exceeds the average by 15 to 30 per cent, and as "over fat" those who exceed by more than 30 per cent, *i.e.* over 155 pounds for a woman 5 feet 3 inches or over 195 pounds for a man 5 feet 8 inches.

Symonds has published* the average relation of height to weight in both men and women at different ages, as computed from the records of accepted applicants for life insurance in the United States and Canada. The results are found in the following tables; that for men being based on 74,162 and that for women on 58,855 cases. In all these cases the height includes shoes and the weight includes ordinary clothing.

SYMONDS'S TABLE OF HEIGHT AND WEIGHT FOR MEN AT DIFFERENT AGES

BASED ON 74,162 ACCEPTED APPLICANTS FOR LIFE INSURANCE

(*Medical Record*)

AGES	15–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69
5 ft. 0 in.	120	125	128	131	133	134	134	134	131	
1 in.	122	126	129	131	134	136	136	136	134	
2 in.	124	128	131	133	136	138	138	138	137	
3 in.	127	131	134	136	139	141	141	141	140	140
4 in.	131	135	138	140	143	144	145	145	144	143
5 in.	134	138	141	143	146	147	149	149	148	147
6 in.	138	142	145	147	150	151	153	153	153	151
7 in.	142	147	150	152	155	156	158	158	158	156
8 in.	146	151	154	157	160	161	163	163	163	162
9 in.	150	155	159	162	165	166	167	168	168	168
10 in.	154	159	164	167	170	171	172	173	174	174
11 in.	159	164	169	173	175	177	177	178	180	180
6 ft. 0 in.	165	170	175	179	180	183	182	183	185	185
1 in.	170	177	181	185	186	189	188	189	189	189
2 in.	176	184	188	192	194	196	194	194	192	192
3 in.	181	190	195	200	203	204	201	198		

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* *Medical Record*, September 5, 1908; and *McClure's Magazine*, January, 1909.

SYMONDS'S TABLE OF HEIGHT AND WEIGHT FOR WOMEN AT DIFFERENT AGES

BASED ON 58,855 ACCEPTED APPLICANTS FOR LIFE INSURANCE

(*McClure's Magazine*)

AGES	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64
4 ft. 11 in.	111	113	115	117	119	122	125	128	128	126
5 ft. 0 in.	113	114	117	119	122	125	128	130	131	129
1 in.	115	116	118	121	124	128	131	133	134	132
2 in.	117	118	120	123	127	132	134	137	137	136
3 in.	120	122	124	127	131	135	138	141	141	140
4 in.	123	125	127	130	134	138	142	145	145	144
5 in.	125	128	131	135	139	143	147	149	149	148
6 in.	128	132	135	137	143	146	151	153	153	152
7 in.	132	135	139	143	147	150	154	157	156	155
8 in.	136	140	143	147	151	155	158	161	161	160
9 in.	140	144	147	151	155	159	163	166	166	165
10 in.	144	147	151	155	159	163	167	170	170	169

From a study of the records of body weight in relation to the mortality records Symonds concludes that among young people the greatest vitality coincides with a weight somewhat above the accepted average, while with middle-aged and elderly people a condition of slightly less than average fatness is most favorable to vitality and longevity. Another way of stating the same facts is: That the average of healthy men and women keep themselves slightly too thin while young, and allow themselves to grow slightly too stout as they grow older.

Evidently, however, the optimum is very near the average of the accepted applicants as shown in the tables, and Symonds uses these figures as standards in his computations and discussions of the influence of overweight and underweight on longevity and on mortality from specific diseases. Symonds's data therefore support the opinion that the average degree of fatness of healthy American people is just about the most advantageous fatness for them to maintain. Whatever we accept as the ideal relation of weight to height, it is obvious that the proper standard for fuel value of the diet is that which will preserve the desired degree of fatness while sustaining the desired amount of activity. If good authorities differ in standards for fuel value, it is because, consciously or unconsciously, they contemplate different amounts of muscular activity or the maintenance of a different physique.

That the amount of food required per day to maintain a healthy adult at the desired body weight will vary considerably with age and size and enormously with extremes of muscular activity has already been explained at some length in Chapter VII and need not be discussed further here. Unless it is desired to increase or decrease the body weight, the optimum energy intake of the healthy adult will be that which coincides with the total energy expenditure; in other words the "standard" and the "requirement" will in this case be the same.

Energy Allowances for Children

Food allowances or dietary standards for children differ from those for adults in that they must provide not only for all expenditures but also for growth. Recently a considerable number of accurate measurements of energy expenditure of children have been made — especially of infants in the first year of life and of boys twelve and thirteen years old. These data whether obtained by the method of direct or indirect calorimetry give precise information as to the energy output at the time of the experiment, but naturally the observations cannot cover the entire 24 hours of the day, nor can experiments of a few hours' duration give any direct information as to how much the intake must exceed the output in order to provide amply for a normal rate of growth. Observations of the unrestricted food consumption (ordinary dietary studies) of healthy children who are making normal growth, and nitrogen balance experiments which show both gain in weight and storage of nitrogen (growth of protein tissue) may be expected to furnish evidence of some value though of a somewhat inferential nature. As a result of compilation and study of all available data whether of dietary studies, nitrogen balance experiments, observations of the respiratory exchange, or direct measurements of energy output, the following standards are suggested:

FOOD ALLOWANCES FOR HEALTHY CHILDREN (GILLETT)

AGE	CALORIES PER DAY	
Years	Boys	Girls
Under 2	900–1200	900–1200
2–3	1000–1300	980–1280
3–4	1100–1400	1060–1360
4–5	1200–1500	1140–1440
5–6	1300–1600	1220–1520
6–7	1400–1700	1300–1600
7–8	1500–1800	1380–1680
8–9	1600–1900	1460–1760
9–10	1700–2000	1550–1850
10–11	1900–2200	1650–1950
11–12	2100–2400	1750–2050
12–13	2300–2700	1850–2150
13–14	2500–2900	1950–2250
14–15	2600–3100	2050–2350
15–16	2700–3300	2150–2450
16–17	2700–3400	2250–2500

In earlier allowances no distinction was made between boys and girls below ten years of age. The averages of recorded data show, however, a slightly higher energy exchange (or metabolism) in boys than in girls of the same age, though the difference is often less than the range allowed to cover differences of size and activity at a given age. Beyond 10 years of age, the energy exchange in boys evidently increases more rapidly than in girls, probably because of their greater restlessness and muscular activity through this period of development and their greater average rate of growth during and after the fifteenth year.

In this connection the accompanying table adapted from that of Manny based on data from Holt, Burt, and Boas is of interest.

Average Weights and Rates of Growth of Boys and Girls at Different Ages (Manny)

Age	Boys				Girls			
	Weight		Increase		Weight		Increase	
	Kgms.	Lbs.	Per Year Lbs.	Per Week Grams	Kgms.	Lbs.	Per Year Lbs.	Per Week Grams
At birth . .	3.43	7.55			3.25	7.16		
6 months . .	7.27	16.00	16.90	147	7.05	15.50	16.68	145
1 year . .	9.32	20.50	9.00	78	9.00	19.80	8.60	75
2 years . .	12.05	26.50	6.00	52	11.59	25.50	5.70	50
3 years . .	14.18	31.20	4.70	41	13.63	30.00	4.50	39
4 years . .	15.91	35.00	3.80	33	15.45	34.00	4.00	35
5 yr. 6 mo. .	18.73	41.20	4.13	36	18.09	39.80	3.87	34
6 yr. 6 mo. .	20.55	45.20	4.00	35	19.73	43.40	3.60	31
7 yr. 6 mo. .	22.50	49.50	4.30	38	21.68	47.70	4.30	38
8 yr. 6 mo. .	24.77	54.50	5.00	44	23.86	52.50	4.80	42
9 yr. 6 mo. .	27.09	59.60	5.10	45	26.09	57.40	4.90	43
10 yr. 6 mo. .	29.73	65.40	5.80	51	28.59	62.90	5.50	48
11 yr. 6 mo. .	32.14	70.70	5.30	46	31.59	69.50	6.60	58
12 yr. 6 mo. .	34.95	76.90	6.20	54	35.77	78.70	9.20	80
13 yr. 6 mo. .	38.55	84.80	7.90	69	40.32	88.70	10.00	87
14 yr. 6 mo. .	43.27	95.20	10.40	91	44.68	98.30	9.60	84
15 yr. 6 mo. .	48.82	107.40	12.20	107	48.50	106.70	8.40	73
16 yr. 6 mo. .	55.00	121.00	13.60	119	51.02	112.30	5.60	49

Children, like adults, will vary in muscular activity and this will influence their energy requirements irrespective of other conditions. Among other conditions to be considered are differences in size and physical development among children of the same age and sex. Children of more than average size, if normally active and not over-fat, will require somewhat more food than an average child of the same age. An estimate of energy requirement per unit of weight at different ages has been given in Chapter VII (page 196). A child who has become somewhat emaciated, either through rapid growth * or other causes, should have a larger food allowance than would ordinarily be required either for his age or for his weight.

In calculating the food requirements of a family it is best not to estimate the needs of other members in terms of that of the man of the family (because men on account of the great differences in activity of their occupations are likely to be more variable in their energy requirements than are children of any given age) but rather to estimate the Calories for each member of the family separately according to his or her own needs and then sum up the total. Not infrequently other members of the family may require more food than the man; especially if he be of less than average size and engaged in sedentary or other light work.

The Problem of a Standard for Protein

In attempting to set a standard for the amount of protein in the dietary we find no such definite and satisfactory basis for judgment as in the case of total food (or fuel) value. There is no indication that any kind of work necessarily increases the

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* Large as are the appetites of growing children it is not uncommon for the "growth impulse" to outrun the food intake so that the child although always having had access to ample food may as the result of very rapid growth be brought into a condition somewhat resembling that of the young animals described in the preceding chapter (page 338) which become emaciated through "attempting to grow" on rations sufficient only for maintenance, *i.e.* through the growth of some tissues at the expense of others. As Aron points out a child in this condition has an abnormally low percentage of fat and high percentage of water in his body content. Hence he needs extra food not only to increase his weight up to that which corresponds to his height, but also to restore the normal percentage of fat in the body weight which he already has.

expenditure of protein as muscular work increases the expenditure of fuel, and the body cannot store up protein to anything like the extent that it stores fuel in the form of fat; the feeding of protein above what is required for maintenance increases only slightly the store of protein which the body carries.

When one writer proposes an amount of protein but little above the minimum required for equilibrium, while another advocates a much larger amount, there is implied a difference of view regarding protein such as no longer exists with respect to the energy metabolism. The difference, it is true, is hardly so great as might appear from a casual examination of the proposed standards. It may perhaps be most fairly expressed in terms of the relation between protein and energy in the different standards. Protein would contribute, according to the standards of Voit, Playfair, and Gautier, about 16 per cent of the fuel value of the food; of Atwater, about 15 per cent; of Langworthy, 12 per cent; of Chittenden, 8½ per cent.

It will be of interest to examine some of the arguments which have been advanced in favor of a high protein or of a low protein diet. The following extracts, given in chronological order, are from writings of those who had given special study to the subject and chiefly from the literature of the first decade of this century, when Chittenden's investigation of the protein requirement was a subject of active discussion. The time of publication of these opinions must not be overlooked, since some of the phenomena then attributed to differences in protein intake might perhaps now be attributed, in part at least, to the ash constituents and vitamines of the food.

Opinions regarding the Value of Liberal Protein Diet

Liebig believed that fats and carbohydrates were burned in the body primarily to supply it with warmth, and that protein alone served as the source of muscular work and other forms of tissue activity. He therefore classed the non-nitrogenous as

" respiratory " and the nitrogenous as " plastic " foodstuffs, and treated the proteins as playing a " nobler " part in nutrition than can be taken by fat or carbohydrate. Although it was soon demonstrated that carbohydrates and fats as well as protein serve the body in the production of muscular energy, yet the influence of Liebig's teaching, and of the great attention given to protein in Voit's classical researches on nutrition, together with the fact that protein is the most prominent constituent of protoplasm, has resulted in a strong tendency to associate high protein feeding with increased stamina and muscular power.

The reasoning of those who appreciated the results of more recent experimental work, and yet believed the general attitude of Liebig and Voit to have been largely sustained by experience, is well expressed by Von Noorden, who wrote in 1893: *

" When one considers that the dietary habits of peoples are the results of biological laws, it would seem that the action of these laws, extending through the thousands of years of existence of the species, would have resulted in the establishment of suitable habits regarding the amounts of protein consumed. The data gathered by Voit may be taken as showing that this normal habit involves the consumption of about 105 grams of digestible protein † per day, a smaller protein consumption being usually associated with weak individuals or inactive peoples. While men can maintain equilibrium on less, still it can rightly be said that a liberal protein consumption makes for a full development of the man. A single individual may for years, or even decades, offend against this biological law unpunished. When, however, the small consumption of protein continues for generations, there results a weak race."

Von Noorden, however, is careful to add:

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* Freely translated from the first edition of Von Noorden's *Pathologie der Stoffwechsel.*

† Corresponding to Voit's allowance of 118 grams of total protein when the food for the sake of economy, as contemplated by Voit, is taken somewhat largely from vegetable sources.

"On the other hand, the importance of protein must not be overestimated. A diet is not necessarily good because the amount of protein is right; it must have the proper proportions of the non-nitrogenous nutrients as well, since the protein is not to be depended upon for the necessary fuel value. Better somewhat less protein with a liberal amount of total food than more protein with insufficient fuel value; the latter brings a rapid loss of strength, the former can be endured very well, at least for a long time, and very likely throughout the life of the individual."

Chittenden, in 1905, had reached exactly the opposite conclusion, — that the products of protein metabolism are a constant menace to the well-being of the body, and that any excess of protein over what the body actually needs is likely to be directly injurious, and at best puts an unnecessary and useless strain upon the liver and kidneys. Chittenden had satisfied himself by his numerous and long-continued experiments that both physical and mental stamina are promoted by decreasing the amount of protein in the food: "Greater freedom from fatigue, greater aptitude for work, greater freedom from minor ailments, have gradually become associated in the writer's mind with this lowered protein metabolism and general condition of physiological economy" . . . (*Physiological Economy in Nutrition*, pages 51, 127).

Hutchison, in 1906, concluded that the normal amount of protein in a diet furnishing 3000 Calories should be placed at about 75 grams. This allows some margin above the results of Chittenden's experiments and agrees with the relation of protein to calories in mother's milk, which Hutchison regards as nature's hint as to the proper balance of nitrogenous and non-nitrogenous food for the human species (*Chemical News*, Vol. 94, page 104).

Folin held that the argument for a high protein diet based on the fact that large amounts of protein are commonly eaten by those who can afford it can be equally well applied to the dietetic use of alcoholic beverages and is no more convincing in one case than in the other; while on the other hand, study of protein metabolism has given rather strong evidence that the body has no need of such amounts as are commonly eaten.

The loss of body nitrogen which occurs in the early periods of restricted protein feeding, and which was not determined nor specifically discussed by Chittenden, is treated by Folin as follows: "All the living protoplasm in the animal organism is suspended in a fluid very rich in protein, and on account of the habitual use of more nitrogenous food than the tissues can use as protein, the organism is ordinarily in possession of approximately the maximum amount of reserve protein in solution that it can advantageously retain. When the supply of food protein is stopped, the excess of reserved protein inside the organism is still sufficient to cause a rather large destruction of protein during the first day or two of protein starvation, and after that the protein catabolism is very small, provided sufficient non-nitrogenous food is available. But even then, and for many days thereafter, the protoplasm of the tissues has still an abundant supply of dissolved protein, and the normal activity of such tissues as the muscles is not at all impaired or diminished. When 30 grams or 40 grams of nitrogen have been lost by an average-sized man during a week or more of abstinence from nitrogenous food (but with an abundance of carbohydrate and fat) the living muscle tissues are still well supplied with all the protein that they can use. . . . The continuous excessive use of protein may lead, however, to an accumulation of a larger amount of reserve protein than the organism can with advantage retain in its fluid media. It is entirely possible that the continuous maintenance of such an unnecessarily large supply of unorganized reserve material may sooner or later weaken one, or another, or all, of the living tissues. At any rate, it seems scarcely conceivable that the human organism, having all the time access to food, can gain in efficiency on account of such an excess of stored protein. The carrying of excessive quantities of fat is considered as an impediment, the carrying of excessive quantities of unorganized protein may be none the less so because more common and less strikingly apparent" (*American Journal of Physiology*, Vol. 13, pages 131–132, 136–137).

Benedict argued that general experience in animal feeding favors the use of liberal quantities of protein, and that "while men may for some months reduce the proportion of protein in their diet very markedly and apparently suffer no deleterious consequences, yet, nevertheless, a permanent reduction of the protein beyond that found to be the normal amount for man is not without possible danger. The fact that a subject can so adjust an artificial diet as to obtain nitrogenous equilibrium with an excretion of nitrogen amounting to about 2 or 3 grams per day is no logical argument for the permanent reduction of the nitrogen in food for the period of a lifetime. . . . Dietary studies all over the world show that in those communities where productive power, enterprise, and civilization are at their highest, man has instinctively and independently selected liberal rather than small quantities of protein" (*American Journal of Physiology*, Vol. 16, page 409).

A similar position was taken by Meltzer, who compared the appetite for a liberal surplus of protein with the liberal way in which the body is provided with organs and tissues for nearly all of its functions, and concludes that "valuable as the facts which Chittenden and his colaborer found may be, they do not make obvious their theory that the minimum supply is the optimum — the ideal. The bodily health and vigor which people with one kidney still enjoy does not make the possession of only one kidney an ideal condition. The finding that the accepted standard of protein diet can be reduced to one half can be compared with the finding that the inspired oxygen can be reduced to one half without affecting the health and comfort of the individual, but no one deduces from the latter fact that the breathing of air so rarefied would be the ideal. . . . The storing away of protein, like the storing away of glycogen and fat, for use in expected and unexpected exceptional conditions is exactly like the superabundance of tissues in an organ of an animal, or like an extra beam in the support of a building or a bridge — a factor of safety" (*Science*, Vol. 25, page 481).

In view of the arguments of Benedict and of Meltzer, it is of especial interest that in his later book Chittenden says: "It is certainly just as plausible to assume that increase in the consumption of protein food follows in the footsteps of commercial and other forms of prosperity, as to argue that prosperity or mental and physical development are the result of an increased intake of protein food. Protein foods are usually costly and the ability of a community to indulge freely in this form of dietetic luxury depends in large measure upon its commercial prosperity." Moreover, Chittenden contends that his allowance of 60 grams of protein per day for a man of average size is a perfectly trustworthy figure, with a reasonable margin of safety; that "dietetic requirements, and standard dietaries, are not to be founded upon the so-called cravings of appetite, but upon reason and intelligence reënforced by definite knowledge of the real necessities of the bodily machinery"; that "we must be ever mindful of the fact, so many times expressed, that protein does not undergo complete oxidation in the body to simple gaseous products like the non-nitrogenous foods, but that there is left behind a residue not so easily disposed of"; and that "there are many suggestions of improvement in bodily health, of greater efficiency in working power, and of greater freedom from disease, in a system of dietetics which aims to meet the physiological needs of the body without undue waste of energy and unnecessary drain upon the functions of digestion, absorption, excretion, and metabolism in general . . . " (*The Nutrition of Man*, pages 160, 164, 227, 269).

Plainly the dietary habit of well-to-do people and the dietary standards which have been generally accepted in the past tend to be decidedly liberal with respect to protein, and to prescribe it in quantities which may be believed to be beneficial but certainly are not known to be necessary. It does not seem advisable, however, to adopt as a standard the lowest amount of protein to which the body can adjust itself, but rather to regard as the normal requirement an amount which will enable the body to maintain not only its equilibrium, but also some such reserve store of protein as we are accustomed to carry. An allowance of about 75 grams of protein per man per day, which is 50 per cent above the average estimate of actual requirement (page 220), seems fully adequate in view of our present knowledge.

A reasonable surplus of protein, from suitable food materials, can hardly be injurious and may be advantageous. Whether such a surplus should be especially recommended or not is largely an economic question. Where little can be spent for food and there is danger that too little food may be eaten, it would be a mistake to use a surplus of protein which could economically be replaced by other food of greater fuel value. In such cases one must not be misled by the popular statement that "protein builds tissue" into supposing that a liberal amount of protein can keep the body strong in spite of a deficiency in the total food. This impression is still somewhat prevalent, but is certainly incorrect.

The body is weakened through getting too little food, because body material must then be burned for fuel. So long as the total food be deficient, the loss of body substance will continue, because not only the food protein, but body tissues as well, must be burned to meet the energy requirement. To strengthen the body through the diet we must increase, not the protein alone, but primarily the total calories.

Strengthening or weakening of the body by feeding ordinarily depends much more upon the sufficiency or insufficiency of the energy value of the total food than upon the amount of protein which it contains.

Protein Standards for Children and for Family Dietaries

Little can be said with confidence regarding the best amount of protein for children after the nursing period. In practice well-planned dietaries for children usually contain between 10 and 15 per cent of the total energy in the form of protein. During the years of rapid growth a considerable fraction of the protein of the food is utilized in the synthesis of body proteins; and since the amount of food protein required to form a gram of body protein is variable, depending upon the amino acid make-up of the former, it is evident that the kind of protein supplied becomes a matter of great importance. Here chemical and physiological laboratory evidence, clinical experience, and its evident place in nature all indicate plainly the superiority of milk as source of supply of protein for growth, whether the case be that of the growing child after weaning or of the nursling fed through the mother. The recommendation that family dietaries should whenever possible include " a quart of milk a day for every child " was aimed primarily to insure an appropriate protein supply. Needless to say, the milk also supplies important amounts of many other substances essential to growth.

Since the energy requirement is greatly increased by muscular activity and the protein requirement is not, it is evident that in the metabolism of normal adults the energy and protein requirements will not run parallel. The protein requirement of the healthy adult depends chiefly upon his size, while his energy requirement depends chiefly upon his activity.

In childhood both the energy requirement and the protein requirement are high — often two to three times as high per unit of weight as for adults without muscular work. Moreover the high protein and energy requirements of the child as compared with the man are found to run approximately parallel and as shown in a previous chapter the same proportion of protein in terms of the total energy which seems rational for the adult dietary suffices also for the food requirements of the child provided in the latter case the food is of appropriate kind.

In most family groups the differences in age and size will constitute a more prominent factor than the differences in activity, and since the former affect energy and protein requirements in about the same proportion, it becomes feasible and convenient to set the protein allowance for ordinary family groups in terms of a proportion of the total food value. To allow for varying conditions and for individual preferences as well as to provide a liberal margin for safety it is customary to consider that from 10 to 15 per cent of the total calories may be in the form of protein.

In cases where the nutritive requirements of growth, pregnancy, or lactation are to be met, the kind of protein is perhaps as important as the amount.

Standards for the Calcium, Phosphorus, and Iron Content of the Dietary

Formerly dietary standards took no account of the ash constituents because it was assumed that dietaries furnishing sufficient energy and protein would always be adequate as regards the "inorganic" elements. As explained in previous chapters this assumption is not safe in the case of calcium, phosphorus, or iron. In the light of present knowledge adequate dietary standards must provide for these elements. The experimental evidence regarding the minimum requirements of the body for each of these elements has been reviewed in earlier chapters and there has been but brief discussion of the relation between minimum and optimum amounts.

The evidence thus far available indicates an average minimum requirement for equilibrium, per man per day, of 0.45 gram calcium (0.63 gram CaO), 0.96 gram phosphorus (2.20 grams P_2O_5), and about 0.010 gram (10 milligrams) of iron.

To allow only these quantities in the daily food would correspond to an allowance of only 50 grams per man per day of protein.

If the standard allowance be set 50 per cent above the indicated average minimum corresponding to an allowance of 75 grams of protein we obtain

Calcium, 0.68 gram (equivalent to 0.95 gram of calcium oxide, CaO).
Phosphorus, 1.44 grams (equivalent to 3.30 grams of P_2O_5).
Iron, 0.015 gram (15 milligrams).

If these be taken as proper allowances per man of 70 kilograms whose energy requirement averages 3000 Calories per day, then the corresponding allowances for other adults or for families containing children could also be stated as follows:

	For Adults per Kilogram of Body Weight	For Children (or Families Containing Children) per 100 Calories
Protein	1.07 grams	2.5 * grams
Phosphorus	0.0206 gram	0.048 gram
Calcium	0.0097 gram	0.023 gram
Iron	0.00022 gram	0.0005 gram

If it be desired to provide as liberal a margin of safety here as in the case of a protein allowance of 100 grams per man per day, then the above figures must obviously be increased by one third.

The Unidentified Essentials

Of the unidentified fat-soluble and water-soluble substances essential to normal metabolism we have as yet no direct quantitative measures, either of the proportions in which they occur in food or are needed in nutrition. In view of their importance

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* In the case of the child this should be mainly milk protein.

it is plain that they should not be ignored in the planning of dietaries, either of children or adults. McCollum and Simmonds have recently shown that a low intake of either " fat soluble A " or " water soluble B " not only retards or suspends the growth of young animals but is also distinctly detrimental to adults. A diet furnishing barely enough of these essentials to support slow growth of young regularly resulted in subnormal vitality when fed to adults; but the symptoms were not always the same, *e.g.* some of the adults lost weight while others maintained weight but lost vitality. They state: " Our results indicate that there is no low plane of intake of either of these substances which can be said to maintain an animal without loss of vitality. When the minimal amount necessary for the prevention of loss of weight is approached, the life of the animal is jeopardized if the diet is persisted in." They also find that " the animal can tolerate being limited to a very low intake of either the dietary A or B much better with an otherwise excellent diet than when it is less well constituted," and also that " it is better to have a liberal supply of one and a minimal supply of the other of the A and B than the minimal allowance of both." The presence of sufficient quantities of these substances is insured by making prominent in the diet the types of foods rich in them. These are chiefly: milk and its products, eggs, vegetables, fruits, and the outer portions of the cereal grains — all foods which it is wise to make prominent in the diet for other reasons as well. It will be remembered that " fat soluble A " and " water soluble B " may or may not occur abundantly in the same articles of food. Milk, eggs, and green vegetables appear to be rich in both; butter in " fat soluble A " and whole grains in " water soluble B." Thus either milk or eggs alone, or both butter and whole grain products, would provide the two kinds of unidentified essentials. When both economy and efficiency are considered, it appears that *milk and vegetables are especially* *worthy of a more prominent place in the diet* than is commonly given them in present American practice.

Limitations of Dietary Standards. — At the risk of repetition let it be clear that too much weight must not be attached to any of the so-called dietary standards, *i.e.* to any attempt to state the requisites of an adequate diet in terms of quantities of certain nutrients. As Atwater sought strongly to emphasize, a dietary standard at best is "only an indication, not a rule." Some of those who have been most active in recent investigation are most emphatic in warning against the expectation that dietary standards can be made to embrace all the qualities which a diet must have in order to be permanently adequate. Thus Hart, McCollum, Steenbock, and Humphrey in a very recent article * say:

"With this recognition of all the normal factors for adequate nutrition there must not simultaneously arise a desire for a mathematical expression of these factors in feeding standards. It is doubtful if this can ever be done, at least for certain of them. For example, the rôle of the mineral nutrients is so varied, including such widely separate functions as construction and control through antagonism, as to make it seem futile to attempt an expression of absolute requirements when natural foods, with their diversity of mineral content, are involved. Even the recognition of differences in the quality of proteins and their relation to nutrition will make it more difficult to continue expressing protein requirements in exact quantities than before the development of such knowledge; and what can be said of the quantitative requirements of fat soluble A and water soluble B and their supply in feeding materials? We need more effort placed on the accumulation of information on the physiological behavior of feeding stuffs than on the attempts to bring out new mathematical expressions of feeding standards."

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* Proceedings of the National Academy of Sciences, Vol. 3, page 374 (May, 1917).

The Economic Use of Food

True economy in the use of food must be physiological as well as pecuniary economy. The diet must supply amply all the requirements of nutrition (not merely the appetite nor the need for energy and protein) and this must be accomplished without the expenditure of too large a proportion of the income. The majority of families in the United States have had in recent normal times incomes of less than $800 per year, of which not over 45 per cent can be spent for food if other living conditions are to be at all satisfactory. This implies an allowance of approximately one dollar per day for food for the "normal" family of five,* or 20 cents per capita per day.

If this be taken as approximating the average expenditure in normal years,† it would follow that the sum annually spent for food in the United States is in the neighborhood of $7,000,000,000. From such statistical estimates of the value of the different food industries as the writer has been able to find it would appear that this is distributed somewhat as follows:

Meats, poultry, fish, and shellfish	about	$2,800,000,000	— or about 40 per cent.
Eggs	about	$400,000,000	— or about 6 per cent.
Milk	about	$500,000,000	— or about 7 per cent.
Cheese	about	$50,000,000	— or less than 1 per cent.
Butter and other fats	about	$500,000,000	— or about 7 per cent.
Grain products	about	$1,000,000,000	— or about 14 per cent.
Sugar, molasses, etc.	about	$500,000,000	— or about 7 per cent.
Vegetables	about	$500,000,000	— or about 7 per cent.
Fruits	about	$300,000,000	— or about 4 per cent.
Nuts ‡	about	$50,000,000	— or less than 1 per cent.
Miscellaneous,§ by difference			about 6 to 7 per cent.

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* If the family of five be reckoned as equivalent in food requirements to 3.7 men, the amount here suggested as available for food would correspond to 27 cents "per man per day" or "per unit."

† No attempt is made in this chapter to quote the fluctuations of prices under war conditions. The economic *relationships* here discussed will be found to be but little disturbed by a general raising or lowering of the level of prices.

‡ This estimate doubtless includes considerable quantities of nuts not used as such for human food but pressed for oil and the residue fed to farm animals.

§ Including beverages, condiments, and minor unclassified food materials.

Any such estimates as these can be no more than rough approximations since they depend upon data which are by no means complete and accurate for the year in which gathered and are subject to fluctuation from year to year. It also appears impossible to avoid arbitrary assumptions regarding the relations of wholesale and retail values. They are intended, therefore, only to indicate in the most general way the relative prominence of expenditure for the different types of food materials as judged from the statistics of the food industries.

Another statistical estimate may be obtained from the data published by the U. S. Bureau of Labor Statistics, who report that of the total value of food consumed in 2567 workingmen's families the distribution of expenditure was as follows:

	PER CENT OF TOTAL COST OF FOOD
Meat, poultry, and fish	33.80
Eggs	5.14
Milk	6.52
Cheese	0.80
Butter and lard	11.66
Grain products	9.57 *
Sugar and molasses	5.34
Vegetables	9.72
Fruit	5.05
Other food and food adjuncts	7.50

These averages are based upon data which were apparently obtained, for the most part at least, by simply asking questions of the housewife regarding the kinds, amounts, and costs of her food purchases and relying upon her memory for the facts. The probable errors in data for individual families would thus be large, but the great number of families included in the inquiry would tend to minimize the errors in the final average.

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* Low partly because of purchase of flour rather than bread, partly because oatmeal, etc., were often not reported under this head but under "other foods."

A different kind of data bearing on this same problem is found in the dietary studies made under the auspices of the United States Department of Agriculture or of the New York Association for Improving the Condition of the Poor. These dietary studies are accurate records of the kinds and amounts of foods consumed by given groups of people during a period of a week or more. From such studies, chiefly of family groups, 208 have been taken as presumably representative of American food habits generally, and the cost of these dietaries has been studied with reference to the distribution of expenditure under headings corresponding to those used in the case of the above statistical estimates with the following results:

	Per Cent of Total Cost of Food
Meats and fish (including poultry and shellfish if used)	34.3
Eggs	5.7
Milk (including cream if used)	9.6
Cheese	1.0
Butter and other fats	8.6
Grain products	17.4
Sugar, molasses, etc.	4.5
Vegetables	10.1
Fruit (and nuts if used)	5.0
Miscellaneous *	3.8

Of the dietaries included in the above average, 92 constituted a series observed during 1914–1915 in connection with the food investigations of the New York Association for Improving the Condition of the Poor. These studies were not entirely confined to New York City nor to families of low incomes. The cost of food per man per day ranged from 12 to 76, averaging 34 cents. The median cost was 31.5 cents per man per day. In

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* Tea, coffee, and other food adjuncts were usually but not always reported under this heading. The reported average is therefore somewhat below the truth.

one fourth of the families the cost was below 25 cents; in one fourth it was above 40 cents; in one half it was between 25 and 40 cents per man per day.

The average distribution of expenditure in these 92 families was as follows:

	Per Cent of Total Cost of Food
Meat and fish (including poultry and shellfish when used)	33.19
Eggs	5.55
Milk (and cream if used)	9.08
Cheese	1.13
Butter and other fats	8.14
Grain products	17.85
Sugar, molasses, etc.	3.80
Vegetables	9.12
Fruit	6.03
Nuts	0.35
Miscellaneous (chiefly beverages, condiments, and other food adjuncts)	5.76

When these 92 studies were grouped according to the amount spent per man per day for food, it was apparent that as the scale of expenditure became more liberal a larger proportion of the money was spent for butter and fruit and a smaller proportion for breadstuffs. The distribution of expenditure among other types of food was, however, very similar in the dietaries of low, medium, and high cost.

Each of the three kinds of evidence used in arriving at the above estimates of distribution of expenditure for food may readily be criticized as inaccurate or inconclusive or both. Yet the trend of the data derived from the different kinds of evidence is so consistent that it can hardly be devoid of significance. It can scarcely be doubted that of the money devoted to the purchase of food the average American family spends from 30 to 40 per cent for meats and fish (including poultry and shellfish when used), about 5 or 6 per cent for eggs, about 7 to 10 per cent for milk, from 7 to 12 per cent for butter and other fats, from 10 to 20 per cent for bread and other cereal and bakery products, 3 to 7 per cent for sugar and other sweets, 7 to 10 per cent for vegetables, 2 to 8 per cent for fruit, and less than 2 per cent for cheese and nuts. At the same time it is plain that such a food budget, however prevalent, need not be regarded as fixed. Many people occasionally, and some habitually, put the last and smallest of the items just mentioned in the place of the first and largest by using cheese or nuts as so-called "meat substitute," more properly as an alternative to meat, — a custom which on the whole appears to be growing. The place of each type of food in the diet has been discussed in a general way elsewhere * and space does not permit us to go over the same ground here.

That the writer does not regard the usual distribution of expenditure for food in American families as being either inevitable or ideal may be indicated by the fact that in his own household, consisting of three adults and four growing children, the distribution of money expended for food is about as follows:

	Per Cent of Total Cost of Food
Meats, poultry, and fish	10–15
Eggs	5–7
Milk	25–30
Cheese	2–3
Butter and other fats	10–12
Bread, cereals, and other grain products	12–15
Sugar, molasses, and syrups	about 3
Vegetables and fruits	15–18

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* Sherman, *Food Products*, pages 74–81, 108–111, 139–141, 212–216, 288–295, 346–351, 357, 388–393, 440–444.

Just what prominence should be given to each type of food in the provisioning of a given family or community is a problem calling for consideration of many factors. One important feature of the problem is to ascertain how the normal distribution of expenditure among the various types of food materials affects the relative proportions of nutrients in the resulting mixed diet. The accompanying table permits a comparison between the expenditures for the different types of food and the returns from each in terms of energy, protein, calcium, phosphorus, and iron in the case of the series of 92 family dietaries described on page 389. In individual dietaries the returns will naturally vary according as an economical or an expensive food of its kind is chosen, but in the average of 92 different dietaries, each of a week's duration, the danger of error due to such individual variations is minimized.

Each Type of Food in Percentage of Total (Average of 92 Dietaries)

	Cost	Calories	Protein	Calcium	Phosphorus	Iron
Meats and fish . .	33.19	16.54	36.29	3.68	26.70	31.43
Eggs	5.55	1.75	4.49	3.25	4.00	6.18
Milk *	9.08	8.11	10.13	50.19	18.52	4.72
Cheese	1.13	0.94	2.08	7.28	2.96	0.55
Butter and other fats	8.14	10.29	0.28	0.67	0.33	0.39
Grain products .	17.85	37.79	35.86	15.31	28.85	24.95
Sugar and molasses	3.80	10.78	0.07	0.69	0.06	0.20
Vegetables . . .	9.12	9.03	8.91	13.25	14.65	26.22
Fruits	6.03	3.87	1.08	4.66	2.41	4.09
Nuts	0.35	0.27	0.22	0.14	0.26	0.18
Miscellaneous . .	5.76	0.65	0.59	0.88	1.26	1.09

If we compare the cost of each type of food with the energy and individual nutrients which it furnishes, we find that because of the differing prominence of the several factors of food value in the various types of food it is often difficult to decide which expenditures were more economical. Thus in the averages just given meat and fish cost one third of the total expenditure

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* Cream, in those cases in which it was purchased, is here included with milk. The amount of cream was small, if any.

for food and furnished about one third of the protein, phosphorus, and iron but only one sixth of the energy and only about one thirtieth of the calcium. Eggs furnished protein, phosphorus, and iron about in proportion to their cost, but less calcium and much less than a proportionate amount of energy. Milk furnished calories and protein about in proportion to cost, twice as much phosphorus, and five times as much calcium in proportion, but only half as much iron.

By adopting the principle of a score card and assigning weights to the different factors of food value, it becomes feasible to compute a "composite valuation" or "score" for each food or group of foods which may then be compared with its cost. Since the most frequent deficiency in American dietaries is inadequacy of total food or energy value and most dietaries actually observed are of such composition as would furnish enough of each essential element if the total amount of food eaten were sufficient to provide a liberal energy supply, it seems reasonable to assign to the energy value of a diet a weight of about half of its composite valuation. It also seems reasonable to assign the remaining "points" equally to protein, calcium, phosphorus, and iron.*

If then we give to energy a weight of 60 on a scale of 100 and to protein, calcium, phosphorus, and iron each a weight of 10, or to energy 40 and to protein, calcium, phosphorus, and iron each 15, we obtain from the data of the table above the "score values" or "composite valuations" under the designations "I" and "II" respectively in the table which follows:

	Cost	"Score Value" or "Composite Valuation"	
		I	II
Meats and fish	33.19	19.73	21.33
Eggs	5.55	2.84	3.39
Milk (and cream)	9.08	13.22	15.78
Cheese	1.13	1.85	2.30
Butter and other fats	8.14	6.34	4.37
Grain products	17.85	33.17	30.85
Sugar and molasses	3.80	6.57	4.47
Vegetables	9.12	11.72	13.07
Fruit	6.03	3.55	3.38
Nuts	0.35	0.24	0.23
Miscellaneous	5.76	0.77	0.83

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* In reality this amounts to giving a higher valuation to the protein since this is counted both as protein and as a part of the energy supply as well.

By comparing the composite valuation with the cost it will be seen that if either of these methods of estimating comparative values is at all valid, the money spent in these 92 families for milk and cheese, grain products, and vegetables brought a better relative return in food value and was therefore in this sense better invested than the money spent for meats and fish, eggs, and fruit.

In making any such comparison it must be kept prominently in mind: (1) that the weights assigned to the different factors of food value must necessarily be more or less arbitrarily chosen so that the resulting "composite valuations" or "food values" rest partly on facts and partly on assumptions; (2) that not all the important factors of food value are taken into account in these valuations, "vitamine values" for instance being wholly omitted from the calculation because as yet we have not the data necessary to permit us to give them numerical expression. It is quite possible that when it becomes feasible to state the vitamine values in numerical terms and give them due weight in the composite valuation, the expenditures for eggs and butter may appear more economical than is indicated by the above table. Any comparisons based on the use of such arbitrary weights or valuations as can at present be assigned must therefore be used with much discretion if misconceptions are to be avoided; but if so used they may be found serviceable in guiding the economical choice of food and to some extent in teaching relative food values.

Individual articles of food may be given "score values" or "composite valuations" in a similar manner. Thus if 100 Calories be given a value of 40 on the scale of 100, and such quantities of protein, phosphorus, calcium and iron as should accompany 100 Calories in an adequate economical diet be given a value of 15 each, the score for almonds might be ascertained as follows:

To every 100 Calories of almonds there are 3.23 grams of protein, 0.071 gram of phosphorus, 0.039 gram of calcium, and 0.0006 gram of iron. If we accept the allowance* of 75 grams of protein, 1.44 grams of phosphorus, 0.68 gram of calcium, and 15 milligrams of iron per man per day, then to every 100 Calories of the 3000 ordinarily taken as the requirement of a man at ordinary labor, there should be 2.5 grams of protein, 0.048 gram of phosphorus, 0.023 gram of calcium, and 0.0005 gram of iron. Then to every 100 Calories of almonds there is 1.3 (3.23 divided by 2.5) times the amount of protein required to "balance" the energy value; 1.48 times the amount of phosphorus, 1.61 times the amount of calcium, and 1.2 times the amount of iron. Scoring these as indicated above, we have the score value for almonds as follows:

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* See page 383.

Assumed Values		Score Points
Calories (100)	40	40
Protein	1.3 × 15	19.5
Phosphorus	1.48 × 15	22.2
Calcium	1.61 × 15	24.2
Iron	1.20 × 15	18.0
		123.9

Since a pound of almonds contains 16.14 100-Calorie portions, then a pound of almonds has a score value of 2000 (123.9 multiplied by 16.14). The following table gives the score value of common typical foods:

APPROXIMATE SCORE VALUE (COMPOSITE VALUATION) PER POUND OF SOME COMMON TYPICAL FOODS AS PURCHASED

	I*	II*		I*	II*
Meat — Beef, sirloin	1290	1460	Grain Products (*Con.*)		
Bacon	1770	1460	Bread, rye	1125	1111
Eggs	1092	1341	Corn meal	1444	1360
Cheese —			Crackers	1579	1433
Cottage	1287	1688	Corn flakes	1270	1090
Hard American	4460	5690	Farina	1418	1308
Milk — Condensed			Flour, graham	2000	2150
sweetened	2000	2200	Flour, rye	1502	1459
unsweetened	1556	1955	Flour, white	1372	1257
Skimmed	500	670	Hominy	1301	1147
Whole	600	700	Macaroni	1502	1444
Butter	2320	1750	Oatmeal	2245	2465
Cream — 18.5% fat	860	860	Rice, white	1289	1139
40% fat	1350	1150	Vegetables —		
Lard	2450	1650	Asparagus, fresh	279	368
Olive oil	2450	1650	Beans, dry, white	2750	3350
Sugar	1090	725	Beans, dry, Limas	2380	2780
Grain Products —			Beans, fresh Limas	363	420
Bread, entire wheat	1250	1320	Beans, string	374	472
Bread, white	1098	1060	Beets	246	286

* The two sets of arbitrary score values correspond to the two systems of "weights" or "points" explained above. The score value will vary slightly with the data of the particular analysis and should perhaps be expressed only in round numbers.

APPROXIMATE SCORE VALUE (COMPOSITE VALUATION) PER POUND OF SOME COMMON TYPICAL FOODS AS PURCHASED — *Continued*

	I*	II*		I*	II*
Vegetables (*Con.*)			Fruit (*Con.*)		
Cabbage	285	367	Bananas	254	236
Carrots	278	338	Dates	1298	1240
Cauliflower	487	640	Grapefruit	167	169
Celery	256	350	Grapes	286	266
Corn, canned	497	523	Lemons	199	228
Cucumbers	125	153	Olives	1000	1000
Lentils	2834	3464	Oranges	209	228
Lettuce	280	380	Peaches, fresh	169	177
Onions	280	330	Pears	236	228
Peas, dry	2510	2960	Pineapple	234	253
Peas, fresh	400	475	Plums	345	337
Parsnips	349	405	Prunes	1144	1135
Potatoes, sweet	399	374	Raisins	1500	1550
Potatoes, white	377	414	Nuts —		
Radishes	161	195	Almonds*	1900	2000
Spinach	630	890	Cocoa	2900	3231
Squash	130	144	Filberts*	1676	1752
Tomatoes	162	192	Peanuts*	2010	2078
Turnips	246	307	Pecans*	1556	1440
Fruit —			Walnuts*	730	670
Apples, fresh	175	156			
Apples, dry	1075	955			

By dividing the "Score Value" of a pound of any food by the price in cents per pound one finds the number of score units or points of food value obtained for each cent, and a comparison of different foods on this basis gives some indication of their relative economy, *if the limitations of such comparisons are held strictly in mind.* Among these limitations may be mentioned (1) the fact already noted that such valuations necessarily involve the arbitrary assignment of weights to the different factors or phases of food value so that facts and assumptions are inseparably combined in the final results notwithstanding the numerical form in which these are expressed; (2) the further tacit assumption that a given amount of protein, of phosphorus, of calcium, or of iron is of the same value in whatever food

* With shell.

found, which is certainly not true in detail and may be very far from true in many cases; (3) that any such attempt to reduce the values of different types of food to a single basis for comparison necessarily tends to obscure those differences of composition and character between the different types of food, which must be kept in mind in order that one may give each type of food its proper place and thus secure a well-balanced dietary.

Let us return then to the consideration of the average data of the 92 dietaries as given in the table on page 391.

The average food value of these 92 dietaries calculated per man per day was as follows:

Energy	2928 Calories
Protein	101 Grams
Calcium	0.72 Gram (1.01 Grams CaO)
Phosphorus	1.52 Grams (3.48 Grams P_2O_5)
Iron	0.0166 Gram

Comparing these averages with the amounts actually required for normal nutrition (page 383) it will be seen that the freely chosen dietaries contained a liberal surplus of protein and a fair supply of phosphorus and iron but scarcely more than is actually necessary of calories or of calcium. Correspondingly we find that the number of individual family dietaries actually deficient in calcium and in total food value (calories) is high enough to cause serious concern, while the cases of deficiency of phosphorus or iron were considerably less frequent and there were few if any cases showing an actual deficiency of protein.

This suggests that there would be true economy in a somewhat different distribution of expenditure by which less should be spent for expensive high protein food, unless it is also rich in calcium or furnishes a high energy value in proportion to its cost, while more prominence should be given to those foods which are rich in calcium or are advantageous sources of energy without being conspicuously poor in phosphorus and iron. In general this would mean somewhat less meat and somewhat more of milk and vegetables, of the cheaper sorts of fruit, and of bread or other grain products in the diet.

Breadstuffs and other staple grain products always give a high energy return as compared with their cost, and usually also a high return in protein and ash constituents, the latter, however, depending largely upon whether " whole grain " or highly milled products are used. In general the more economical the dietary must be the higher should be the proportion of expenditure for bread (or other grain products) and the more restricted the dietary the more desirable it becomes to use " whole grain " rather than highly milled products.

Meats give usually, as compared with their cost, a fair return in protein, phosphorus, and iron, a low return in energy, and an extremely low return in calcium. Milk, on the other hand, is very rich in calcium and furnishes in proportion to its cost more energy and phosphorus than does meat of average fatness, and proteins and iron of at least equal value if not of equal amount. Milk also excels other foods in respect to the advantageous quantitative relationships of its ash constituents and is probably the best possible source of the growth-promoting substances needed by all young mammals. The well-known dietary rule of " a quart of milk a day for every child," already amply justified by practical results, has received additional support from several angles through the recent advances in our knowledge of the chemistry of nutrition.

Armsby estimates that of the energy value of grain about 18 per cent is recovered for human consumption in milk and only about 3.5 per cent in beef.

While milk is somewhat poor in iron, that which it contains is exceptionally efficient in nutrition. Moreover, the supply of this element may readily be safeguarded either by the use of whole grain products or by increasing the proportion of fruits and vegetables in the diet. It will be recalled from what has been said in earlier chapters that an abundance of fruits and vegetables in the diet is also advantageous in other important ways. Vegetables and some fruits, economically selected, bring a good return in nutrients for the money expended and their liberal use adds greatly to both the attractiveness and the wholesomeness of the diet.

It therefore seems advisable to spend at least as much for fruit and vegetables as for meat and fish; also to spend at least as much for milk as for meat (or for milk and cheese as for meat and fish).

At ordinary prices eggs are about as cheap a food as meat, and cheese (like milk) is much cheaper than meat in proportion to its food value. Eggs and cheese can therefore be substituted for meat to any extent desired in the individual dietary without detriment to its nutritive value and usually with good economy.

General adoption of a dietary such as we now believe to be best would call for more milk and perhaps more vegetables and fruit than now come to our city markets; but more of these foods will be produced and marketed as the demand for them increases. Moreover an increased demand for these foods and a correspondingly decreased (per capita) demand for meat, so far from causing any serious "dislocation of industry," will help to facilitate natural evolution of American agriculture. With increasing population on stationary area farming necessarily becomes more intensive. Beef is produced less by the grazing of cattle on free ranges of unbroken prairie and more by the feeding of grain and other cultivated crops. For a given amount of food consumed a dairy herd yields a product of greater food value than does a herd of beef animals. An increasing ratio of milch cows to beef cattle is naturally to be expected with the development of a more intensive agriculture and will be to the advantage of producer and consumer alike. In regions adapted to dairy farming but too remote from large markets to ship in the fresh state we may anticipate an increasing production of condensed and dried milk and of butter and cheese. An increased production of fruit and vegetables should also be a natural result of a more stable and intensive agriculture. At the same time the concentration of population in large cities increases the expense of transportation and makes the cost of retail distribution a serious item, especially in the case of bulky products with a relatively low value per pound. Cabbage, potatoes, and root crops can be produced at a low cost per ton, but the percentage of the cost of production which must be added when they are distributed through modern retail agencies tends constantly to increase.

The more highly perishable fruits and vegetables having a higher cost per pound or ton are now successfully transported in transcontinental carload shipments. Precooling and lowered temperatures in refrigerator cars, secured by the use of salt with ice, promise to reduce still further the losses incident to their transportation.

Cold storage tends to equalize prices throughout the season on such perishable foods as butter, cheese, and eggs, and secures a supply of other fresh foods such as apples, of good quality, throughout almost the entire year. With the perfection of facilities for more rapid distribution in cities after removal from freezing temperatures the number and quantity of vegetables and fruits so preserved should increase greatly. The canning industry has already developed to enormous proportions and it seems likely that drying processes will be applied to a constantly increasing number of the more bulky vegetables.

The physical and economic wastes in marketing are being reduced by various agencies in the United States Department of Agriculture, now largely consolidated in the Bureau of Markets, and in general the supply may be trusted to keep pace with the demand in the gradual shifting of emphasis from meat toward dairy products, vegetables, and fruit, which seems to be clearly desirable both in view of our present knowledge of nutrition, and in the light of our agricultural situation.

The broader and more accurate conception of food values which is made possible by the recent advances in the chemistry of food and nutrition will guide the judgment both as to the proper emphasis to be placed upon each type of foods in the dietary and as to the wise selection among foods of the same type. It supplies the economic justification for the purchase of certain foods which would appear expensive if considered simply as sources of proteins, fats, and carbohydrates, and, on the other hand, it shows that some foods which are economical sources of protein and energy are also of high nutritive value in other respects.

Making due allowance for all known factors which affect the nutritive value of foods, there remain large discrepancies between nutritive value and market cost, and correspondingly ample opportunity for the exercise of true economy in the choice of food materials.

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APPENDICES

APPENDIX A

NOMENCLATURE AND CLASSIFICATION OF PROTEINS

Joint Recommendations of the Committees on Protein Nomenclature of the American Physiological Society and American Society of Biological Chemists

SINCE a chemical basis for the nomenclature of the proteins is at present not possible, it seemed important to recommend few changes in the names and definitions of generally accepted groups, even though, in many cases, these are not wholly satisfactory. The recommendations are as follows:

First. — The word " proteid " should be abandoned.

Second. — The word " protein " should designate that group of substances which consist, so far as at present is known, essentially of combinations of α-amino acids and their derivatives, *e.g.* α-amino acetic acid or glycocoll; α-amino propionic acid or alanine; phenyl-α-amino propionic acid or phenylalanine; guanidin-α-amino valerianic acid or arginine, etc., and are therefore essentially polypeptids.

Third. — That the following terms be used to designate the various groups of proteins:

I. SIMPLE PROTEINS. — Protein substances which yield only α-amino acids or their derivatives on hydrolysis.

Although no means are at present available whereby the chemical individuality of any protein can be established, a number of simple proteins have been isolated from animal and vegetable tissues which have been so well characterized by constancy of ultimate composition and uniformity of physical properties that they may be treated as chemical individuals until further knowledge makes it possible to characterize them more definitely.

The various groups of simple proteins may be designated as follows:

(*a*) *Albumins.* — Simple proteins soluble in pure water and coagulable by heat.

(*b*) *Globulins.* — Simple proteins insoluble in pure water, but soluble in neutral solutions of salts of strong bases with strong acids.*

(*c*) *Glutelins.* — Simple proteins insoluble in all neutral solvents but readily soluble in very dilute acids and alkalies.†

(*d*) *Alcohol-soluble Proteins.* — Simple proteins soluble in relatively strong alcohol (70–80 per cent), but insoluble in water, absolute alcohol, and other neutral solvents.‡

(*e*) *Albuminoids.* — Simple proteins which possess essentially the same chemical structure as the other proteins, but are characterized by great insolubility in all neutral solvents.§

(*f*) *Histones.* — Soluble in water and insoluble in very dilute ammonia, and, in the absence of ammonium salts, insoluble even in an excess of ammonia; yield precipitates with solutions of other proteins and a coagulum on heating which is easily soluble in very dilute acids. On hydrolysis they yield a large number of amino acids, among which the basic ones predominate.

(*g*) *Protamins.* — Simpler polypeptids than the proteins included in the preceding groups. They are soluble in water, uncoagulable by heat, have the property of precipitating aqueous solutions of other proteins, possess strong basic properties, and form stable salts with strong mineral acids. They yield comparatively few amino acids, among which the basic amino acids greatly predominate.

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* The precipitation limits with ammonium sulphate should not be made a basis for distinguishing the albumins from the globulins.

† Such substances occur in abundance in the seeds of cereals and doubtless represent a well-defined group of simple proteins.

‡ The subclasses defined (*a, b, c, d*) are exemplified by proteins obtained from both plants and animals. The use of appropriate prefixes will suffice to indicate the origin of the compounds, *e.g.* ovoglobulin, myoalbumin, etc.

§ These form the principal organic constituents of the skeletal structure of animals and also their external covering and its appendages. This definition does not provide for gelatin, which is, however, an artificial derivative of collagen.

II. CONJUGATED PROTEINS. — Substances which contain the protein molecule united to some other molecule or molecules otherwise than as a salt.

(*a*) *Nucleoproteins.* — Compounds of one or more protein molecules with nucleic acid.

(*b*) *Glycoproteins.* — Compounds of the protein molecule with a substance or substances containing a carbohydrate group other than a nucleic acid.

(*c*) *Phosphoproteins.* — Compounds of the protein molecule with some, as yet undefined, phosphorus-containing substance other than a nucleic acid or lecithin.*

(*d*) *Hemoglobins.* — Compounds of the protein molecule with hematin or some similar substance.

(*e*) *Lecithoproteins.* — Compounds of the protein molecule with lecithins (lecithans, phosphatids).

III. DERIVED PROTEINS.

1. *Primary Protein Derivatives.* — Derivatives of the protein molecule apparently formed through hydrolytic changes which involve only slight alterations of the protein molecule.

(*a*) *Proteans.* — Insoluble products which apparently result from the incipient action of water, very dilute acids, or enzymes.

(*b*) *Metaproteins.* — Products of the further action of acids and alkalies whereby the molecule is so far altered as to form products soluble in very weak acids and alkalies, but insoluble in neutral fluids.

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* The accumulated chemical evidence distinctly points to the propriety of classifying the phosphoproteins as conjugated compounds, *i.e.* they are possibly esters of some phosphoric acid or acids and protein.

This group will thus include the familiar "acid proteins" and "alkali proteins," not the salts of proteins with acids.

(*c*) *Coagulated Proteins.* — Insoluble products which result from (1) the action of heat on their solutions, or (2) the action of alcohols on the protein.

2. *Secondary Protein Derivatives.*[*] — Products of the further hydrolytic cleavage of the protein molecule.

(*a*) *Proteoses.* — Soluble in water, uncoagulated by heat, and precipitated by saturating their solutions with ammonium sulphate or zinc sulphate.[†]

(*b*) *Peptones.* — Soluble in water, uncoagulated by heat, but not precipitated by saturating their solutions with ammonium sulphate.[‡]

(*c*) *Peptids.* — Definitely characterized combinations of two or more amino acids, the carboxyl group of one being united with the amino group of the other, with the elimination of a molecule of water.[§]

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[*] The term "secondary hydrolytic derivatives" is used because the formation of the primary derivatives usually precedes the formation of these secondary derivatives.

[†] As thus defined, this term does not strictly cover all the protein derivatives commonly called proteoses, *e.g.* heterproteose and dysproteose.

[‡] In this group the kyrins may be included. For the present we believe that it will be helpful to retain this term as defined, reserving the expression "peptid" for the simpler compounds of definite structure, such as dipeptids, etc.

[§] The peptones are undoubtedly peptids or mixtures of peptids, the latter term being at present used to designate those of definite structure.

APPENDIX B

COMPOSITION OF FOODS

Explanation of Headings

FOOD as purchased may or may not consist entirely of edible material. When an article of food contains inedible matter or refuse, this may be stated separately and the composition of the edible portion then given, or the percentages of refuse and of edible nutrients in the original matter may be given so as to show directly the percentage of each edible nutrient obtained in the material as purchased. For example; 100 pounds of beef contains 16 pounds of bone and 84 pounds of moist flesh, of which 15.4 pounds are protein, 15 pounds fat, 53 pounds water, and 0.6 pound ash. The composition may be stated in either of the following forms:

COMPOSITION OF BEEF

REFUSE PER CENT	WATER PER CENT	PROTEIN PER CENT	FAT PER CENT	ASH PER CENT
16.0	53.0	15.4	15.0	0.6

COMPOSITION OF BEEF

REFUSE	EDIBLE PORTION			
Per Cent	Water Per Cent	Protein Per Cent	Fat Per Cent	Ash Per Cent
16.0	63.1	18.3	17.9	0.7

For most purposes it is convenient to include in one table the nutrients calculated both on the basis of edible material and of material as purchased. In such a case the percentage of refuse in the material as purchased may be given or may be omitted as in the following form:

COMPOSITION OF BEEF

	WATER	PROTEIN	FAT	ASH
Edible portion (E. P.)	63.1	18.3	17.9	0.7
As purchased (A. P.)	53.0	15.4	15.0	0.6

In order to avoid confusion and possible errors in taking data from tables of composition it is important to note in which form the percentages are stated. Data given in either form are of course readily convertible into the other. In Table I which follows, the percentages of nutrients and the corresponding energy values are stated in the form last illustrated above. Table II shows percentages of ash constituents in the edible portion only. Table III shows grams of protein and of calcium, phosphorus, and iron in 100-Calorie portions, which estimates may obviously be used equally well whether the food be originally recorded in terms of edible material or of material as purchased.

A word of explanation regarding the sources and reliability of the data may also be offered. The percentages of proteins, fats, and carbohydrates given in Table I are in the great majority of cases taken from the tables of composition of American food materials compiled by Atwater and Bryant and published in Bulletin 28 of the Office of Experiment Stations, U. S. Department of Agriculture. By reference to this bulletin the reader may find the number of analyses on which the average is based and the maximum and minimum of the recorded percentages of each constituent, as well as the percentages of moisture, ash, and in some cases crude fiber. The energy values given in Table I are computed from the average percentage of protein, fat, and carbohydrate by the use of the latest and most accurate factors (see page 143). The data for ash constituents given in Tables II and III are based on a critical compilation of all available ash analyses, both American and European. In some cases only a single ash analysis could be found; in other cases the data given are averages of many fairly concordant analyses. Between these extremes are data of all degrees of probable reliability. It does not seem feasible to indicate the relative accuracy of the estimates for different articles of food. In general it may be said that only in the cases of the more important foods are the ash analyses as yet sufficiently numerous and concordant to justify one in laying great emphasis upon comparisons of one article of food with another. More emphasis can properly be laid upon estimates of the ash constituents of rations or dietaries made up of several food materials, since in such cases accidental errors will tend to offset each other. It is chiefly to facilitate such calculations that the tables have been made as complete as seemed practicable even though this necessitated including estimates of differing reliability on apparently equal terms.

Data which are based in part at least upon assumptions are inclosed in parenthesis. They are not necessarily less accurate as estimates of average composition than are some of the directly determined data of individual analyses.

Since many unpublished ash analyses have been included in the present averages, Tables II and III will be found to present many differences in detail from those published elsewhere, or in the first edition of this book. The general trend of the averages has, however, not been materially altered by the results of recent work.

Attention may also be called to the fact that in Table II the data are uniformly given as percentages of the elements and not of their oxides. For the convenience of those who may prefer to continue to calculate calcium and phosphorus in terms of the oxides as has been customary in the past, Table III shows the weights of CaO and P_2O_5 as well as of protein, calcium, phosphorus, and iron in 100-Calorie portions of foods.

TABLE I

Edible Organic Nutrients and Fuel Values of Foods[*]

Food		Protein $(N \times 6.25)$ per cent	Fat per cent	Carbohydrate per cent	Fuel Value per Pound Calories	100 Calorie Portion Grams
Almonds	E. P.[†]	21.0	54.9	17.3	2940	15
	A. P.[†]	11.5	30.2	9.5	1615	28
Apples	E. P.	.4	.5	14.2	285	159
	A. P.	.3	.3	10.8	214	212
Apricots	E. P.	1.1	—	13.4	263	174
	A. P.	1.0	—	12.6	247	184
Artichoke, French	E. P.	3.4	.5	12.0	300	151
	A. P.	1.7	.3	6.0	150	302
Asparagus, fresh	A. P.	1.8	.2	3.3	100	450
cooked	A. P.	2.1	3.3	2.2	213	213
Avocado	E. P.	2.1	20.1	7.4	993	46
	A. P.	1.4	13.2	4.8	652	70
Bacon, smoked	E. P.	10.5	64.8	—	2840	16
	A. P.	9.5	59.4	—	2372	19
Bananas	E. P.	1.3	.6	22.0	447	101
	A. P.	.8	.4	14.3	290	156
Barley, pearled		8.5	1.1	77.8	1615	28
Beans, dried		22.5	1.8	59.6	1565	29
Lima, dried		18.1	1.5	65.9	1586	29
Lima, fresh	E. P.	7.1	.7	22.0	557	82
	A. P.	3.2	.3	9.9	250	182

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[*] The percentages of nutrients are taken from Bull. 28, Office of Experiment Stations, U. S. Department of Agriculture. The fuel values are calculated from these percentages by the use of the factors explained in Chapter V, viz. — protein, 4 calories; fat, 9 calories; carbohydrate, 4 calories per gram.

[†] E. P. signifies edible portion; A. P. signifies as purchased.

TABLE I — *Continued*

Food		Protein (N×6.25) per cent	Fat per cent	Carbo-hydrate per cent	Fuel Value per Pound Calories	100 Calorie Portion grams
Beans — *Continued*						
string, fresh	E. P.	2.3	.3	7.4	184	241
	A. P.	2.1	.3	6.9	176	259
baked, canned	A. P.	6.9	2.5	19.6	583	78
red kidney, canned . . .		7.0	.2	18.5	471	96
Beef, brisket, medium fat .	E. P.	15.8	28.5	—	1449	31
	A. P.	12.0	22.3	—	1130	40
chuck, average	E. P.	19.2	15.4	—	978	46
	A. P.	15.8	12.5	—	797	58
corned, average	E. P.	15.6	26.2	—	1353	34
	A. P.	14.3	23.8	—	1230	37
cross ribs, average . . .	E. P.	15.9	28.2	—	1440	32
	A. P.	13.8	24.8	—	1262	36
dried, salted, and smoked,	E. P.	30.0	6.5	.4	817	56
	A. P.	26.4	6.9	—	760	60
flank, lean	E. P.	20.8	11.3	—	838	54
	A. P.	20.5	11.0	—	821	55
fore quarter, lean . . .	E. P.	18.9	12.2	—	842	54
	A. P.	14.7	9.5	—	655	69
fore shank, lean	E. P.	22.0	6.1	—	647	70
	A. P.	14.0	3.9	—	414	110
heart	E. P.	16.0	20.4	1.0	1140	40
	A. P.	14.8	24.7	.9	1292	35
hind quarter, lean . . .	E. P.	20.0	13.4	—	907	50
	A. P.	16.7	11.2	—	757	60
hind shank, lean . . .	E. P.	21.9	5.4	—	617	75
	A. P.	9.1	2.2	—	255	179
hind shank, fat	E. P.	20.4	18.8	—	1171	40
	A. P.	9.9	9.1	—	552	83
liver	E. P.	20.4	4.5	1.7	584	78
	A. P.	20.2	3.1	2.5	537	85
loin	E. P.	19.7	12.7	—	877	52
	A. P.	17.1	11.1	—	764	60
neck, lean	E. P.	21.4	8.4	—	732	62
	A. P.	15.1	5.9	—	493	93
neck, medium fat . . .	E. P.	20.1	16.5	—	1040	44
	A. P.	14.5	11.9	—	749	61

TABLE I — *Continued*

FOOD		PROTEIN (N×6.25) PER CENT	FAT PER CENT	CARBOHYDRATE PER CENT	FUEL VALUE PER POUND CALORIES	100 CALORIE PORTION GRAMS
Beef — *Continued*						
plate, lean	E. P.	15.6	18.8	—	1051	43
	A. P.	13.0	15.5	—	867	52
Porterhouse steak	E. P.	21.9	20.4	—	1230	37
	A. P.	19.1	17.9	—	1077	42
rib rolls, lean	A. P.	20.2	10.5	—	795	57
ribs, lean	E. P.	19.6	12.0	—	845	54
	A. P.	15.2	9.3	—	654	69
ribs, fat	E. P.	15.0	35.6	—	1721	26
	A. P.	12.7	30.6	—	1480	31
round, lean	E. P.	21.3	7.9	—	709	64
	A. P.	19.5	7.3	—	649	70
round, free from visible fat		23.2	2.5	—	512	87
rump, lean	E. P.	20.9	13.7	—	940	49
	A. P.	19.1	11.0	—	796	57
rump, fat	E. P.	16.8	35.7	—	1763	26
	A. P.	12.9	27.6	—	1361	33
sides, lean	E. P.	19.3	13.2	—	890	51
	A. P.	15.5	10.6	—	715	64
sirloin steak	E. P.	18.9	18.5	—	1099	41
	A. P.	16.5	16.1	—	960	48
sweetbreads	A. P.	16.8	12.1	—	799	57
tenderloin	A. P.	16.2	24.4	—	1290	35
tongue	E. P.	18.9	9.2	—	717	63
	A. P.	14.1	6.7	—	529	86
Beets, cooked	E. P.	2.3	.1	7.4	180	252
fresh	E. P.	1.6	.1	9.7	209	217
	A. P.	1.3	.1	7.7	167	271
Blackberries	A. P.	1.3	1.0	10.9	262	173
Blackfish	E. P.	18.7	1.3	—	393	116
	A. P.	7.4	.7	—	163	279
Bluefish	E. P.	19.4	1.2	—	402	113
	A. P.	10.0	.6	—	206	220
Boston crackers		11.0	8.5	71.1	1835	25
Brazil nuts	E. P.	17.0	66.8	7.0	3162	14
	A. P.	8.6	33.7	3.5	1591	28

TABLE I — *Continued*

FOOD		PROTEIN (N×6.25) PER CENT	FAT PER CENT	CARBO-HY-DRATE PER CENT	FUEL VALUE PER POUND CALO-RIES	100 CALORIE PORTION GRAMS
Bread, Boston brown . . .		6.0	6.3	54.0	1345	34
graham		8.9	1.8	52.1	1189	38
rolls, water		9.0	3.0	54.2	1268	36
toasted		11.5	1.6	61.2	1385	33
white, homemade . . .		9.1	1.6	53.3	1199	38
milk		9.6	1.4	51.1	1158	39
Vienna		9.4	1.2	54.1	1199	38
average white		9.2	1.3	53.1	1182	38
whole wheat		9.7	.9	49.7	1113	41
Buckwheat flour		6.4	1.2	77.9	1580	29
Butter		1.0	85.0	—	3491	13
Buttermilk		3.0	.5	4.8	162	280
Butternuts	E. P.	27.9	61.2	3.5	3065	15
	A. P.	3.8	8.3	.5	417	109
Cabbage	E. P.	1.6	.3	5.6	143	317
	A. P.	1.4	.2	4.8	121	376
Calf's-foot jelly		4.3	—	17.4	394	115
Carrots, fresh	E. P.	1.1	.4	9.3	204	221
	A. P.	.9	.2	7.4	158	286
Cauliflower	A. P.	1.8	.5	4.7	139	328
Celery	E. P.	1.1	.1	3.3	84	542
	A. P.	.9	.1	2.6	68	672
Celery soup, canned . . .		2.1	2.8	5.0	243	187
Cerealine		9.6	1.1	78.3	1640	28
Chard	E. P.	3.2	.6	5.0	173	262
Cheese, American pale . .		28.8	35.9	.3	1990	23
American red		29.6	38.3	—	2102	22
Cheddar		27.7	36.8	4.1	2080	22
cottage		20.9	1.0	4.3	499	91
full cream		25.9	33.7	2.4	1890	24
Fromage de Brie . . .		15.9	21.0	1.4	1170	39
Neufchâtel		18.7	27.4	1.5	1484	31
pineapple		29.9	38.9	2.6	2180	21
roquefort		22.6	29.5	1.8	1645	28
Swiss		27.6	34.9	1.3	1945	23
Cherries, fresh	E. P.	1.0	.8	16.7	354	128
	A. P.	.9	.8	15.9	337	134

TABLE I — *Continued*

FOOD		PROTEIN (N×6.25) PER CENT	FAT PER CENT	CARBOHYDRATE PER CENT	FUEL VALUE PER POUND CALORIES	100 CALORIE PORTION GRAMS
Cherries — *Continued*						
canned	A. P.	1.1	.1	21.1	407	112
Chestnuts, fresh	E. P.	6.2	5.4	42.1	1098	41
	A. P.	5.2	4.5	35.4	920	49
Chicken, broilers	E. P.	21.5	2.5	—	493	92
	A. P.	12.8	1.4	—	289	157
Chocolate		12.9	48.7	30.3	2768	16
Cocoa		21.6	28.9	37.7	2258	20
Cod, dressed	A. P.	11.1	.2	—	209	217
salt	E. P.	25.4	.3	—	473	96
	A. P.	19.0	.4	—	361	126
Consommé, canned . . .	A. P.	2.5	—	.4	53	862
Corn, green, canned . . .		2.8	1.2	19.0	455	102
sweet, fresh	E. P.	3.1	1.1	19.7	459	99
	A. P.	1.2	.4	7.7	178	255
Corn meal		9.2	1.9	75.4	1620	28
Cowpeas, dried		21.4	1.4	60.8	1550	29
green	E. P.	9.4	.6	22.7	603	76
Crackers, butter	A. P.	9.6	10.1	71.6	1887	23
cream	A. P.	9.7	12.1	69.7	1938	23
graham	A. P.	10.0	9.4	73.8	1905	24
soda	A. P.	9.8	9.1	73.1	1875	24
water	A. P.	10.7	8.8	71.9	1855	24
Cranberries	A. P.	.4	.6	9.9	212	212
Cream		2.5	18.5	4.5	883	50
Cucumbers	E. P.	.8	.2	3.1	79	575
	A. P.	.7	.2	2.6	68	666
Currants, fresh		1.5	—	12.8	259	175
dried Zante		2.4	1.7	74.2	1455	31
Dandelion greens		2.4	1.0	10.6	277	164
Dates, dried	E. P.	2.1	2.8	78.4	1575	29
	A. P.	1.9	2.5	70.6	1416	32
Doughnuts		6.7	21.0	53.1	1941	23
Eggplant	E. P.	1.2	.3	5.1	126	349
Eggs, uncooked	E. P.	13.4	10.5	—	672	68
	A. P.	11.9	9.3	—	594	76

Table I — *Continued*

Food		Protein (N×6.25) per cent	Fat per cent	Carbo-hydrate per cent	Fuel Value per Pound Calories	100 Calorie Portion Grams
Farina		11.0	1.4	76.3	1640	28
Figs, dried		4.3	.3	74.2	1437	32
Flounder	A. P.	5.4	.3	—	110	412
	E. P.	14.2	.6	—	282	161
Flour, rye		6.8	.9	78.7	1590	29
wheat, California fine		7.9	1.4	76.4	1585	29
wheat, entire		13.8	1.9	71.9	1630	28
wheat, graham		13.3	2.2	71.4	1628	28
wheat, patent baker's grade		13.3	1.5	72.7	1623	28
wheat, straight grade		10.8	1.1	74.8	1608	28
wheat, average high and medium		11.4	1.0	75.1	1610	28
wheat, average low grade		14.0	1.9	71.2	1625	28
Fowls	E. P.	19.3	16.3	—	1017	45
	A. P.	13.7	12.3	—	752	60
Gelatin		91.4	.1	—	1660	27
Grape butter		1.2	.1	58.5	1088	42
Grapes	E. P.	1.3	1.6	19.2	437	104
	A. P.	1.0	1.2	14.4	328	138
Grapefruit	E. P.	.6	.1	12.2	235	193
	A. P.	.4	.1	8.9	172	264
Haddock	E. P.	17.2	.3	—	324	140
	A. P.	8.4	.2	—	160	283
Halibut steaks	E. P.	18.6	5.2	—	550	83
	A. P.	15.3	4.4	—	457	100
Ham, fresh, lean	E. P.	25.0	14.4	—	1042	44
	A. P.	24.8	14.2	—	1030	44
fresh, medium	E. P.	15.3	28.9	—	1458	31
	A. P.	13.5	25.9	—	1303	35
smoked, lean	E. P.	19.8	20.8	—	1209	38
	A. P.	17.5	18.5	—	1073	42
Herring, whole	E. P.	19.5	7.1	—	644	70
	A. P.	11.2	3.9	—	362	125
smoked	E. P.	36.9	15.8	—	1315	35
	A. P.	20.5	8.8	—	731	62
Hominy		8.3	.6	79.0	1609	28

TABLE I — *Continued*

FOOD		PROTEIN (N×6.25) PER CENT	FAT PER CENT	CARBOHYDRATE PER CENT	FUEL VALUE PER POUND CALORIES	100 CALORIE PORTION GRAMS
Honey		.4	—	81.2	1481	31
Huckleberries		.6	.6	16.6	336	135
Kohl-rabi	E. P.	2.0	.1	5.5	140	324
Koumiss		2.8	2.1	5.4	234	194
Lamb, breast	E. P.	19.1	23.6	—	1311	35
	A. P.	15.4	19.1	—	1058	43
chops, broiled	E. P.	21.7	29.9	—	1614	28
fore quarter	E. P.	18.3	25.8	—	1385	33
	A. P.	14.9	21.0	—	1127	40
hind quarter	E. P.	19.6	19.1	—	1149	40
	A. P.	16.5	16.1	—	953	48
leg, roast		19.7	12.7	—	876	52
side	E. P.	17.6	23.1	—	1263	36
	A. P.	14.1	18.7	—	1015	45
Lard, refined		—	100.0	—	4080	11
Lemon juice		—	—	9.8	178	255
Lemons	E. P.	1.0	.7	8.5	201	226
	A. P.	.7	.5	5.9	140	323
Lettuce	E. P.	1.2	.3	2.9	87	525
	A. P.	1.0	.2	2.5	72	633
Liver, beef	E. P.	20.4	4.5	1.7	583	78
	A. P.	20.2	3.1	2.5	538	84
veal	E. P.	19.0	5.3	—	562	81
Lobster, whole	E. P.	16.4	1.8	.4	379	120
	A. P.	5.9	.7	.2	139	326
canned	A. P.	18.1	1.1	.5	382	119
Macaroni		13.4	.9	74.1	1625	28
Macaroons		6.5	15.2	65.2	1922	24
Mackerel	E. P.	18.7	7.1	—	629	72
	A. P.	10.2	4.2	—	356	127
salt	E. P.	21.1	22.6	—	1305	35
	A. P.	16.3	17.4	—	1005	45
Marmalade, orange		.6	.1	84.5	1548	29
Milk, condensed, sweetened		8.8	8.3	54.1	1480	31
skimmed		3.4	.3	5.1	167	273
whole		3.3	4.0	5.0	314	145

TABLE I — *Continued*

FOOD		PROTEIN (N×6.25) PER CENT	FAT PER CENT	CARBOHYDRATE PER CENT	FUEL VALUE PER POUND CALORIES	100 CALORIE PORTION GRAMS
Mince meat, commercial		6.7	1.4	60.2	1280	36
homemade		4.8	6.7	32.1	942	48
Molasses, cane		2.4	—	69.3	1302	35
Mushrooms	A. P.	3.5	.4	6.8	204	223
Muskmelons	E. P.	.6	—	9.3	180	252
	A. P.	.3	—	4.6	89	510
Mutton, fore quarter	E. P.	15.6	30.9	—	1543	29
	A. P.	12.3	24.5	—	1223	37
hind quarter	E. P.	16.7	28.1	—	1450	31
	A. P.	13.8	23.2	—	1197	38
leg	E. P.	19.8	12.4	—	863	52
	A. P.	16.5	10.3	—	718	63
side	A. P.	13.0	24.0	—	1215	37
	E. P.	16.2	29.8	—	1512	30
Nectarines	E. P.	.6	—	15.9	299	152
	A. P.	.6	—	14.8	280	162
Oatmeal		16.1	7.2	67.5	1811	25
Okra	E. P.	1.6	.2	7.4	172	264
	A. P.	1.4	.2	6.5	152	300
Olives, green	E. P.	1.1	27.6	11.6	1357	33
	A. P.	.8	20.2	8.5	995	46
ripe	E. P.	1.7	25.0	4.3	1130	40
	A. P.	1.4	21.0	3.5	947	48
Onions, fresh	E. P.	1.6	.3	9.9	220	206
	A. P.	1.4	.3	8.9	199	228
Oranges	E. P.	.8	.2	11.6	233	195
	A. P.	.6	.1	8.5	169	268
Oxtail soup, canned	A. P.	3.8	.5	4.2	166	274
Oysters	E. P.	6.2	1.2	3.7	228	199
in shell	A. P.	1.2	.2	.7	43	1065
canned	A. P.	8.8	2.4	3.9	328	138
Parsnips	E. P.	1.6	.5	13.5	294	154
	A. P.	1.3	.4	10.8	236	192
Pea soup, canned	A. P.	3.6	.7	7.6	232	196
Peaches, canned	A. P.	.7	.1	10.8	213	213
fresh	E. P.	.7	.1	9.4	188	242
	A. P.	.5	.1	7.7	153	297

TABLE I — *Continued*

FOOD		PROTEIN (N×6.25) PER CENT	FAT PER CENT	CARBOHYDRATE PER CENT	FUEL VALUE PER POUND CALORIES	100 CALORIE PORTION GRAMS
Peanuts	E. P.	25.8	38.6	24.4	2490	18
	A. P.	19.5	29.1	18.5	1877	24
Pears, fresh	E. P.	.6	.5	14.1	288	158
	A. P.	.5	.4	12.7	256	177
Peas, canned	A. P.	3.6	.2	9.8	252	180
dried		24.6	1.0	62.0	1611	28
green	E. P.	7.0	.5	16.9	454	100
	A. P.	3.6	.2	9.8	252	180
Peppers, green	E. P.	1.1	.1	4.6	109	417
Persimmons	E. P.	.8	.7	31.5	615	74
Pies, apple		3.1	9.8	42.8	1233	37
custard		4.2	6.3	26.1	806	56
lemon		3.6	10.1	37.4	1156	39
mince		5.8	12.3	38.1	1300	35
squash		4.4	8.4	21.7	817	56
Pineapples, fresh	E. P.	.4	.3	9.7	196	232
canned	A. P.	.4	.7	36.4	695	65
Pine nuts (pignolias)		33.9	49.4	6.9	2757	16
Pistachios, shelled		22.3	54.0	16.3	2900	16
Plums	E. P.	1.0	—	20.1	383	118
	A. P.	.9	—	19.1	363	125
Pomegranates	E. P.	1.5	1.6	19.5	447	102
Pork, chops, medium	E. P.	16.6	30.1	—	1530	30
	A. P.	13.4	24.2	—	1230	37
chuck ribs and shoulder	E. P.	17.3	31.1	—	1585	29
	A. P.	14.1	25.5	—	1298	35
fat, salt	A. P.	1.9	86.2	—	3555	13
sausage	A. P.	13.0	44.2	1.1	2030	22
side	E. P.	9.1	55.3	—	2423	19
	A. P.	8.0	49.0	—	2145	21
tenderloin	A. P.	18.9	13.0	—	875	52
Potato chips	A. P.	6.8	39.8	46.7	2598	17
Potatoes, white, raw	E. P.	2.2	.1	18.4	378	120
	A. P.	1.8	.1	14.7	302	149
sweet, raw	E. P.	1.8	.7	27.4	558	81
	A. P.	1.4	.6	21.9	447	102

TABLE I — *Continued*

FOOD		PROTEIN (N×6.25) PER CENT	FAT PER CENT	CARBO-HY-DRATE PER CENT	FUEL VALUE PER POUND CALO-RIES	100 CALORIE PORTION GRAMS
Prunes, dried	E. P.	2.1	—	73.3	1368	33
	A. P.	1.8	—	62.2	1160	39
Pumpkins	E. P.	1.0	.1	5.2	117	389
	A. P.	.5	.1	2.6	60	753
Radishes	E. P.	1.3	.1	5.8	133	341
	A. P.	.9	.1	4.0	91	488
Raisins	E. P.	2.6	3.3	76.1	1562	29
	A. P.	2.3	3.0	68.5	1407	32
Raspberries, red		1.0	—	12.6	247	184
black		1.7	1.0	12.6	300	151
Rhubarb	E. P.	.6	.7	3.6	105	433
	A. P.	.4	.4	2.2	63	714
Rice		8.0	.3	79.0	1591	29
Salmon, dressed	A. P.	13.8	8.1	—	582	78
whole	E. P.	22.0	12.8	—	923	49
	A. P.	15.3	8.9	—	642	71
Sausage, Bologna	E. P.	18.7	17.6	.3	1061	43
	A. P.	18.2	19.7	—	1135	40
farmer	E. P.	29.0	42.0	—	2240	20
	A. P.	27.9	40.4	—	2156	21
Shad, whole	E. P.	18.8	9.5	—	727	61
	A. P.	9.4	4.8	—	367	124
roe		20.9	3.8	2.6	582	78
Shredded wheat		10.5	1.4	77.9	1660	27
Spinach, fresh	A. P.	2.1	.3	3.2	109	417
Squash	E. P.	1.4	.5	9.0	209	217
	A. P.	.7	.2	4.5	103	443
Strawberries		1.0	.6	7.4	169	269
Succotash, canned		3.6	1.0	18.6	444	102
Sugar		—	—	100.0	1815	25
Tomatoes, fresh	A. P.	.9	.4	3.9	104	438
canned	A. P.	1.2	.2	4.0	103	443
Tuna (tunny fish)	E. P.	26.6	11.4	—	946	48
Turkey	E. P.	21.1	22.9	—	1320	34
	A. P.	16.1	18.4	—	1042	43
sandwich, canned		20.7	29.2	—	1568	29

TABLE I — *Continued*

Food		Protein (N×6.25) per cent	Fat per cent	Carbohydrate per cent	Fuel Value per Pound Calories	100 Calorie Portion grams
Turnips	E. P.	1.3	.2	8.1	178	256
	A. P.	.9	.1	5.7	124	367
Veal, breast	E. P.	20.3	11.0	—	817	56
	A. P.	15.3	8.6	—	629	72
cutlet	E. P.	20.3	7.7	—	683	66
	A. P.	20.1	7.5	—	670	68
fore quarter	E. P.	20.0	8.0	—	690	66
	A. P.	15.1	6.0	—	517	88
hind quarter	E. P.	20.7	8.3	—	715	64
	A. P.	16.2	6.6	—	534	85
side	E. P.	20.2	8.1	—	697	65
	A. P.	15.6	6.3	—	539	84
Vegetable soup, canned		2.9	—	.5	62	735
Walnuts, California or English	E. P.	18.4	64.4	13.0	3199	14
	A. P.	4.9	17.3	3.5	859	53
black	E. P.	27.6	56.3	11.7	3011	15
	A. P.	7.2	14.6	3.0	780	59
Watermelons	E. P.	.4	.2	6.7	136	332
	A. P.	.2	.1	2.7	57	800
Wheat, cracked		11.1	1.7	75.5	1635	28
Whitefish	E. P.	22.9	6.5	—	680	67
	A. P.	10.6	3.0	—	315	144
Zwieback		9.8	9.9	73.5	1915	24

TABLE II

ASH CONSTITUENTS OF FOODS IN PERCENTAGE OF THE EDIBLE PORTION

(Compiled from Various Sources)

FOOD	CALCIUM (Ca)	MAGNESIUM (Mg)	POTASSIUM (K)	SODIUM (Na)	PHOSPHORUS (P)	CHLORINE (Cl)	SULPHUR (S)	IRON (Fe)
Almonds	.239	.251	.741	.019	.465	.037	.160	.0039
Apples	.007	.008	.127	.011	.012	.005	.006	.0003
dried	.032	.037	(.623)	(.050)	.048	(.025)	?	(.0015)
Apricots	.014	.010	.248	.038	.025	.002	.010	(.0003)
dried	(.066)	(.047)	(1.157)	(.177)	(.117)	(.009)	?	(.0014)
Asparagus . . .	.025	.011	.196	.007	.039	.039	.041	.0010
Bacon (See Meat)								
Bananas	.009	.028	.401	.034	.031	.125	.010	.0006
Barley, entire . .	.043	.131	.477	.076	.400	.016	.153	.0041
pearled . . .	.020	(.070)	(.241)	(.037)	.181	(.016)	(.120)	(.0020)
Beans, dried . .	.160	.156	1.229	.097	.471	.032	.215	.0070
kidney, dry . .	.132	.139	1.144	.041	.475	.041	.227	.0072
Lima, dry . .	.071	.188	1.741	.249	.338	.026	.161	.0070
Lima, fresh . .	.028	(.070)	(.613)	(.088)	.133	(.009)	(.057)	.0020
string, fresh . .	.046	.025	.247	.019	.052	.024	.030	.0011
Beef (See Meat)								
Beer	.004	.008	.058	.013	.028	.006	.015	.0001
Beets	.029	.021	.353	.093	.039	.058	.016	.0006
Blackberries . . .	.017	.021	.169	(.007)	.034	(.010)	.020	.0006
Blood (avg.) . .	.008	.004	.075	.261	.031	.280	.137	.0526
Blueberries . . .	.020	.007	.051	.016	.008	.008	.011	.0009
Bluefish (See Fish)								
Bread,								
Boston brown .	.129	.078	(.232)	(.394)	.185	(.607)	.201	(.0030)
"entire wheat" .	(.05)	(.05)	(.208)	(.394)	(.175)	(.607)	(.120)	(.0016)
graham . . .	(.05)	(.05)	(.291)	(.394)	(.218)	(.607)	.150	(.0025)
rye	.024	.039	.151	.701	.148	1.025	.104	(.0016)
white	.027	.023	.108	(.394)	.093	(.607)	.105	.0009
Breadfruit . . .	.084	.007	.235	.027	.068	.100	.049	
Brussels sprouts .	.027	.040	.375	.004	.120	.040	.194	(.0011)
Buckwheat flour .	.039	.048	.130	.027	.226	.012	.071	.0012
Butter	.015	.001	.014	(.788)	.017	(1.212)	(.010)	.0002
Buttermilk . . .	.105	.016	.151	.064	.097	.099	.026	.00025

TABLE II — *Continued*

FOOD	CALCIUM (Ca)	MAGNESIUM (Mg)	POTASSIUM (K)	SODIUM (Na)	PHOSPHORUS (P)	CHLORINE (Cl)	SULPHUR (S)	IRON (Fe)
Cabbage	.045	.015	.247	.027	.029	.024	.066	.0011
Cabbage greens .	.106	.030	.512	.025	.099	.068	.173	.0018
Cantaloupe . . .	.017	.012	.235	.061	.015	.041	.014	.0003
Capers	.122	.022	.209	.051	.062	—	—	—
Carp (See Fish)								
Carrots	.056	.021	.287	.101	.046	.036	.022	.0006
Cauliflower . . .	.123	.014	.222	.068	.061	.050	.086	.0006
Caviar	.137	.022	.422	.874	.176	1.819	—	—
Celery	.078	.014	.316	.084	.037	.156	.022	.0005
Chard	.150	.071	.318	.086	.040	.039	.124	(.0025)
Cheese	.931	.037	.089	.606	.683	.880	.263	.0013
Cherries	.019	.016	.213	.023	.031	.014	.011	.0004
Cherry juice . .	.017	.011	.200	.013	.018	.003	.006	(.0003)
Chestnuts . . .	.034	.051	.560	.065	.093	.006	.068	.0007
Chicken (See Meat)								
Chocolate . . .	.092	(.293)	(.563)	.012	.455	(.051)	.085	(.0027)
Cider	.008	.011	.095	.020	.009	.006	.006	(.0002)
Citron	.121	.018	.210	.011	.033	.003	.020	—
Clams, round . .	.106	.098	.131	.705	.046	1.220	.224	—
soft, long . . .	.124	.079	.212	.500	.122	.910	.213	—
Cocoa	.112	.420	.900	.059	.709	.051	.203	.0027
Coconut, dried . .	.059	.059	.597	.073	.155	.239	(.056)	—
fresh	.024	.020	.300	.036	.074	.120	.028	—
Coconut milk . .	.020	.009	.144	—	.010	—	.008	—
Cod (See Fish)								
Corn (maize), mature	.020	.121	.339	.036	.283	.045	.151	.0029
meal	.018	.084	.213	.039	.190	.146	.111	.0009
sweet	.006	.033	.113	.040	.103	.014	.046	.0008
sweet, dried . .	.021	.121	.414	.146	.376	.050	.167	.0029
Cotton-seed meal .	.265	.462	1.390	.234	1.193	.037	.485	—
Cowpeas	.100	.208	1.402	.161	.456	.040	.240	—
Crackers	.022	.011	.100	(.594)	.102	(.910)	.125	.0015
Cranberries . . .	.018	.007	.077	.010	.013	.009	.007	.0006
Cream	.086	.010	.126	.035	.067	.080	.030	.00022
Cucumbers . . .	.016	.009	.140	.010	.033	.030	.020	.0002
Currants, dried .	.082	.044	.873	.081	.195	.060	.044	(.0025)
fresh	.026	.017	.211	.007	.038	.006	.014	.0005

TABLE II — *Continued*

Food	Calcium (Ca)	Magnesium (Mg)	Potassium (K)	Sodium (Na)	Phosphorus (P)	Chlorine (Cl)	Sulphur (S)	Iron (Fe)
Currant juice . .	.021	.010	.185	(.006)	.018	.004	.005	—
Dandelion . . .	.105	.036	.461	.168	.072	.099	.017	.0027
Dates	.065	.069	.611	.055	.056	.228	.070	.0030
Duck (See Meat)								
Eggplant	.011	.015	(.140)	(.010)	.034	.024	.016	.0005
Eggs	.067	.011	.140	.143	.180	.106	.195	.0030
Egg white . . .	.015	.010	.160	.156	.014	.155	.216	.0001
Egg yolk	.137	.016	.115	.075	.524	.094	.166	.0086
Endive	.104	.013	.380	.109	.038	.167	.035	—
Farina	.021	.025	.120	.065	.125	.076	.155	.0008
Figs, dried . . .	.162	.071	.964	.046	.116	.043	.056	.0030
fresh	.053	.022	.303	.012	.036	.014	.010	—
Fish *								
Flaxseed	.204	.252	.901	.050	.627	.022	.170	—
Flour, buckwheat .	.010	.048	.130	.027	.176	.012	.071	.0012
"entire wheat" .	.031	(.090)	(.274)	(.037)	.238	(.070)	(.180)	.0025
graham . . .	.039	(.133)	(.457)	(.037)	.364	(.070)	.183	.0037
white	.020	.018	.115	.060	.092	.074	.177	.0010
rye	.018	.081	.463	.019	.289	.055	.123	.0013
Fowl (See Meat)								
Gluten feed . . .	.247	.221	.250	.420	.542	.090	.558	—
Goose (See Meat)								
Gooseberries . .	.035	.014	.197	.038	.031	—	.011	.0005
Grapefruit . . .	.021	.009	.161	.004	.020	.005	.010	.0003
Grapejuice . . .	.011	.009	.106	.005	.011	.002	.009	.0003
Grapes	.019	.010	.197	.015	.031	.005	.024	.0003
Guava	.014	.008	.384	—	.030	.045	—	—
Haddock (See Fish)								
Halibut (See Fish)								
Ham (See Meat)								
Hazelnuts . . .	.287	.140	.618	.019	.354	.067	.198	.0041
Herring (See Fish)								
Hominy	.011	.058	.174	.020	.144	.046	(.136)	(.0009)

* Average fish is estimated to contain **per 100 grams of protein** as follows: 0.109 gram Ca; 0.133 gram Mg; 1.671 grams K; 0.373 gram Na; 1.148 grams P; 0.528 gram Cl; 1.119 grams S; 0.0055 gram Fe.

TABLE II — *Continued*

FOOD	CALCIUM (Ca)	MAGNESIUM (Mg)	POTASSIUM (K)	SODIUM (Na)	PHOSPHORUS (P)	CHLORINE (Cl)	SULPHUR (S)	IRON (Fe)
Honey	.004	.018	.386	.001	.019	.029	.001	.0007
Horseradish . . .	.096	.039	.468	.062	.076	.016	.190	—
Huckleberries . .	.020	.007	.051	.016	.008	.008	.011	.0009
Huckleberry wine	.009	.004	.042	.006	.004	.001	.006	—
Jam *								
Jelly	.014	(.010)	(.100)	(.013)	.008	(.004)	(.007)	(.0003)
Kohl-rabi . . .	.077	.030	.370	.050	.071	.053	.057	.0006
Lamb (See Meat)								
Leeks	.058	.014	.199	.081	.006	.024	.072	—
Lemons	.036	.007	.175	.004	.022	.002	.011	.0006
Lemon juice . . .	.024	.010	.127	.009	.010	.003	.006	—
Lemon, sweet . .	.030	.006	.442	—	.042	.013	.016	—
Lentils, dry . . .	.107	.101	.877	.062	.438	.050	.277	.0086
Lettuce	.043	.017	.339	.027	.042	.074	.014	.0007
Limes	.055	.014	.350	.062	.036	.039	.010	—
Lime juice . . .	—	—	—	—	—	—	.003	—
Linseed meal . .	.413	.432	1.083	.251	.741	.085	.396	—
Lupins, dry . . .	.191	.191	.840	.073	.520	.034	—	—
Macaroni . . .	.022	.037	.130	.008	.144	.073	.172	.0012
Mackerel (See Fish)								
Mamey	.009	.012	.345	—	.028	.140	—	—
Mango	.021	.007	.235	—	.017	.019	.013	—
Mangolds . . .	.026	.030	.334	.071	.038	.082	.026	—
Maple syrup . .	.107	.034	.208	.010	.013	(.010)	(.005)	(.003)
Meat †								
Meat extract, solid	.085	.363	7.347	2.394	2.800	3.117	—	—
Meat peptone . .	.025	.124	2.440	.641	1.130	.561	.222	—
Milk (cow's), whole	.120	.012	.143	.051	.093	.106	.034	.00024
(cow's), skimmed	(.122)	(.012)	(.149)	(.052)	(.096)	(.110)	(.035)	.00025
(cow's), condensed . . .	(.300)	(.032)	(.374)	(.134)	.235	(.280)	(.090)	.0006

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* The percentages of the ash constituents in jams are believed to average about two thirds those of the corresponding fruits.

† Average meat is estimated to contain per 100 grams protein as follows: 0.058 gram Ca; 0.118 gram Mg; 1.694 grams K; 0.421 gram Na; 1.078 grams P; 0.378 gram Cl; 1.146 grams S; 0.0150 gram Fe.

TABLE II — *Continued*

Food	Calcium (Ca)	Magnesium (Mg)	Potassium (K)	Sodium (Na)	Phosphorus (P)	Chlorine (Cl)	Sulphur (S)	Iron (Fe)
Milk — *Cont.*								
buffalo	.203	.016	.099	.038	.125	.062	—	—
camel's	.143	.021	.114	.019	.098	.105	—	—
goat's	.128	.013	.145	.079	.103	.014	.037	—
human	.034	.005	.047	.010	.015	.035	—	—
mare's	.083	.007	.081	.010	.054	.029	—	—
sheep's	.207	.008	.187	.030	.123	.071	—	—
Millet	.014	.167	.290	.085	.327	.019	—	—
Molasses	.211	.068	1.349	.019	.044	.317	.129	.0073
Mushrooms	.017	.016	.384	.027	.108	.021	.051	—
Muskmelon	.017	.012	.235	.061	.015	.041	.014	.0003
Mustard	.492	.260	.761	.056	.755	.016	1.230	—
Mutton (See Meat)								
Oatmeal	.069	.110	.344	.062	.392	.069	.202	.0038
Okra	.071	.010	.035	.043	.019	—	—	—
Olives	.122	.002	1.526	.128	.014	.004	.027	.0029
Onions	.034	.016	.178	.016	.045	.021	.070	.0006
Oranges	.045	.012	.177	.012	.021	.006	.011	.0002
Orange juice	.029	.011	.182	.008	.016	.003	.009	.0002
Oysters	.052	.037	.091	.459	.155	.590	.187	.0045
Paprika	.229	.164	2.075	.178	.341	.155	—	—
Parsnips	.059	.034	.518	.004	.076	.030	.036	.0006
Peaches	.016	.010	.214	.022	.024	.004	.009	.0003
dried	.034	.056	(.830)	.082	.146	—	.212	(.0012)
Peanuts	.071	.180	.654	.050	.399	.056	.224	.0020
Pears	.015	.011	.132	.016	.026	.011	.010	.0003
Pear juice	.009	.008	.140	—	.011	—	.009	—
Peas, dried	.084	.149	.903	.104	.400	.035	.219	.0057
fresh	.028	.038	.285	.013	.127	.024	.063	.0017
Pecan nuts	.089	.152	(.332)	—	.335	.050	.113	.0026
Pepper, green, fresh	.006	.010	(.139)	—	.026	.013	.014	.0004
Pepper, black, dry	.440	.156	1.140	.131	.188	.312	—	—
Pepper, white, dry	.425	.113	—	—	.233	.029	—	—
Perch (See Fish)								
Persimmons	.022	.009	.292	.011	.021	.002	.005	—
Pineapple	.018	.011	.321	.016	.028	.051	.009	.0005
Plums	.020	.011	.203	.019	.032	.002	.009	.0005

TABLE II — *Continued*

Food	Calcium (Ca)	Magnesium (Mg)	Potassium (K)	Sodium (Na)	Phosphorus (P)	Chlorine (Cl)	Sulphur (S)	Iron (Fe)
Pomegranate . .	.011	.005	.063	.085	.105	.003	—	.0004
Pork (See Meat)								
Potatoes	.014	.028	.429	.021	.058	.038	.030	.0013
sweet	.019	.028	.397	.039	.045	.094	.024	.0005
Prunes, dried . .	.054	.055	1.030	.069	.105	.017	.037	.0030
Pumpkin	.023	.008	(.320)	.065	.059	—	.021	(.0008)
Radishes . . .	.021	.012	.218	.069	.029	.054	.041	.0006
Raisins	.064	.083	.820	.133	.132	.082	.051	.0021
Raspberries . . .	.049	.024	.173	—	.052	—	.017	.0006
Raspberry juice .	.021	.016	.134	.005	.012	—	.009	—
Rhubarb	.044	.017	.325	.025	.031	.036	.013	.0010
Rice, brown . . .	—	—	—	—	.207	—	—	.0020
white	.009	.033	.070	.025	.096	.054	.117	.0009
Romaine (salad) .	.045	.032	.306	.016	.053	.073	.019	—
Rutabagas . . .	.074	.018	.399	.083	.056	.058	.083	—
Rye, entire . . .	.055	.130	.453	.035	.385	.025	.170	.0039
(See also Bread and Flour)								
Salmon (See Fish)								
Sapato	.026	.008	.179	—	.006	.087	—	—
Shredded wheat .	.041	.144	—	—	.324	—	—	.0045
Shrimp	.096	—	—	—	—	—	—	—
Soup, canned . .	.036	—	.033	—	.030	—	—	—
canned vegetable	.025	.013	.101	—	.038	—	.025	—
Spinach	.067	.037	.774	.125	.068	.074	.038	.0036
Squash, summer, seeds removed	.018	.008	.150	.002	—	—	—	(.0006)
with seeds . .	.024	.012	.180	.004	—	—	—	(.0006)
Squash, winter . .	.019	.011	.320	.004	—	—	—	(.0006)
Strawberries . .	.041	.019	.147	.050	.028	.006	.014	.0008
Tamarind . . .	.007	.021	—	—	.072	.007	.009	—
Tapioca	.023	—	—	—	.090	.018	.029	.0016
Tomatoes . . .	.011	.010	.275	.010	.026	.034	.014	.0004
Tomato juice . .	.006	.010	.310	.015	.015	.055	—	—
Truffles	.024	.018	.404	.077	.062	.039	—	—
Turnips	.064	.017	.338	.056	.046	.041	.065	.0005
Turnip tops . .	.347	.028	.307	.082	.049	.168	.069	—

TABLE II — *Continued*

FOOD	CALCIUM (Ca)	MAGNESIUM (Mg)	POTASSIUM (K)	SODIUM (Na)	PHOSPHORUS (P)	CHLORINE (Cl)	SULPHUR (S)	IRON (Fe)
Veal (See Meat)								
Vinegar (cider) .	.016	.008	.165	—	.013	—	.017	(.0003)
Walnuts	.089	.134	(.332)	—	.358	.040	.172	.0021
Water cress . . .	.187?	.034	.287	.099	.005	.061	.167	.0019
Watermelon . .	.011	.003	.073	.008	.003	.008	.007	
Wheat, entire . .	.045	.133	.473	.039	.423	.068	.181	.0050
(See also Bread and Flour)								
Wheat bran . . .	.120	.511	1.217	.154	1.215	.090	.247	.0078
Wheat germ . .	.071	.342	.296	.722	1.050	.070	.325	—
Wheat gluten . .	.078	.045	.007	.028	.200	.050	.920	—
Whey	.044	.008	.157	.038	.035	.119	.009	?
Whortleberries, entire	.031	.021	.261	.021	.042	—	—	—
flesh only . . .	.020	.011	.087	—	.018	—	—	—
Wine (avg.) . . .	.009	.010	.104	.008	.015	.011	.015	(.0003)

TABLE III

PROTEIN, CALCIUM, PHOSPHORUS, AND IRON IN GRAMS PER 100 CALORIES OF FOOD MATERIAL

(Estimated from data compiled from various sources)

FOOD	PROTEIN	CALCIUM (Ca)	PHOSPHORUS (P)	IRON (Fe)	CaO	P_2O_5
	Grams	Grams	Grams	Grams	Grams	Grams
Almonds	3.22	.037	.072	.00060	.052	.165
Apples	0.64	.012	.020	.00048	.016	.045
Apricots	1.90	.023	.044	.00052	.033	(.100)
Asparagus	8.10	.122	.177	.00451	.171	.405
Bacon (See Meat)						

TABLE III — *Continued*

FOOD	PROTEIN	CALCIUM (Ca)	PHOSPHORUS (P)	IRON (Fe)	CaO	P_2O_5
	Grams	Grams	Grams	Grams	Grams	Grams
Bananas	1.32	.009	.031	.00061	.012	.072
Beans, dried	6.52	.047	.137	.00203	.065	.314
kidney	5.83	(.040)	(.143)	(.00216)	(.056)	(.326)
Lima	5.80	.020	.096	.00200	.028	.221
string	5.55	.110	.126	.00265	.154	.289
Beef (See Meat)						
Beer	—	.008	.061	.00217	.011	.140
Beets	3.47	.064	.084	.00130	.089	.193
Blackberries	2.25	.029	.058	.00104	.042	.133
Blueberries	(0.8)	(.027)	(.011)	(.0012)	(.038)	(.025)
Bluefish (See Fish)						
Bread, Boston brown	2.64	.056	.082	(.0013)	.079	.187
"entire" wheat	3.95	(.020)	.071	(.00065)	(.028)	(.163)
graham	3.42	(.020)	.084	(.00096)	(.028)	(.192)
rye	3.54	.009	.058	.00039	.013	.133
white	3.50	.011	.035	.00035	.015	.081
Brussels sprouts	(7.30)	(.086)	(.380)	(.00349)	(.121)	(.870)
Buckwheat flour	1.85	.011	.065	.00034	.015	.148
Butter	0.13	.002	.002	.00003	.003	.005
Buttermilk	8.40	.294	.271	.00070	.411	.621
Cabbage	5.07	.143	.092	.00349	.200	.210
Cantaloupe	1.51	.044	.038	.00071	.061	.088
Carp (See Fish)						
Carrots	2.42	.124	.101	.00133	.173	.232
Cauliflower	5.90	.403	.200	.00197	.564	.459
Celery	1.28	.421	.201	.00270	.589	.460
Chard	8.37	.393	.105	(.00655)	.550	.240
Cheese	6.05	.212	.156	.00030	.297	.357
Cherries	1.20?	.025	.039	.00051	.035	.090
Chestnuts	2.55	.014	.044	.00029	.019	.088
Chicken (See Meat)						
Chocolate	2.11	.015	.075	(.00044)	.021	.171
Citron	0.15	.037	.010	.00099	.052	.023
Clams, long	19.82	.285	.282	(.00970)	.399	.645
round	14.01	.229	.100	(.00970)	.321	.228
Cocoa	4.35	.023	.143	.00054	.032	.327
Coconut	0.95	.006	.018	(.00030)	.009	.041
Cod (See Fish)						

TABLE III — *Continued*

FOOD	PROTEIN	CALCIUM (Ca)	PHOSPHORUS (P)	IRON (Fe)	CaO	P_2O_5
	Grams	Grams	Grams	Grams	Grams	Grams
Corn	3.06	.006	.102	.00079	(.008)	(.233)
Corn meal	2.59	.005	.053	.0003	.007	.121
Cotton-seed meal	12.80	.066	.298	—	.092	.682
Cowpeas	6.20	.029	.132	—	.041	.303
Crackers, "soda"	2.37	.006	.025	.00036	.008	.057
Cranberries	0.85	.039	.027	.00129	.054	.062
Cream, 18.5 per cent fat . .	1.27	.050	.044	.0001	.072	.100
40 per cent fat	0.58	.020	.020	.00005	.032	.045
Cucumbers	4.60	.090	.191	.00115	.126	.437
Currants, dried (Zante) . .	0.75	.026	.061	.00087	.036	.139
fresh	2.62	.045	.066	.00087	.063	.150
Dandelion greens	3.93	.172	.117	.0044	.241	.269
Dates	0.60	.019	.016	.00086	.026	.037
Duck (See Meat) .						
Eggplant	4.30	.041	.122	.00184	.057	.280
Eggs	9.05	.045	.122	.00205	.063	.279
Egg white	24.12	.020	.022	.00020	.028	.050
Egg yolk	4.32	.036	.118	.00230	.050	.270
Farina	3.05	.006	.035	.00022	.008	.079
Figs	1.35	.051	.037	.00095	.072	.084
Fish (See footnote on page 423)						
Flour, buckwheat	1.84	.011	.065	.00034	.015	.148
"entire" wheat	3.85	.009	.066	.0007	.012	.152
graham	3.71	.011	.101	.00100	.015	.232
white (wheat)	3.20	.006	.026	.00023	.008	.060
rye	1.95	.005	.082	.00037	.007	.188
Fowl (See Meat)						
Goose (See Meat)						
Grapefruit	1.15	.040	.036	.00058	.056	.083
Grapes	1.35	.019	.032	.00031	.027	.074
Grapejuice	0.35	(.011)	.011	.0003	.015	.025
Haddock (See Fish)						
Halibut (See Fish)						
Ham (See Meat)						
Hazelnuts	—	.041	.050	.00057	.057	.115
Herring (See Fish)						
Hominy	2.35	.002	.027	.00025	.002	.063

TABLE III — *Continued*

FOOD	PROTEIN	CALCIUM (Ca)	PHOSPHORUS (P)	IRON (Fe)	CaO	P_2O_5
	Grams	Grams	Grams	Grams	Grams	Grams
Honey	0.12	.002	.006	.0003	.002	.013
Huckleberries	0.82	.027	.011	.0012	.038	.025
Kohl-rabi	6.48	.249	.186	.00194	.349	.426
Lamb (See Meat)						
Lemons	2.25	.081	.049	.00135	.113	.112
Lemon juice	—	.060	—	—	.084	.059
Lentils	7.37	.031	.126	.00247	.043	.288
Lettuce	6.27	.224	.224	.00785	.314	.513
Linseed meal	—	—	—	—	—	—
Lupins	—	—	—	—	—	—
Macaroni	3.70	.006	.040	.00033	.008	.092
Mackerel (See Fish)						
Maple syrup	—	.037	(.003)	(.001)	.053	(.007)
Meat (See footnote on page 424)						
Milk, whole	4.75	.174	.134	.00035	.243	.308
skimmed	9.25	(.331)	.262	(.00068)	(.463)	(.600)
condensed, sweetened	2.70	(.096)	.072	(.0002)	(.135)	.165
condensed, unsweetened	5.75	.189	.146	(.0004)	(.264)	.335
Molasses	0.83	.074	.015	.00255	.102	.035
Muskmelon	1.51	.043	.038	.0008	.060	.088
Mutton (See Meat)						
Oatmeal	4.20	.017	.099	.00096	.024	.226
Olives	0.37	.041	.004	.00097	.057	.010
Onions	3.30	.069	.093	.0010	.097	.212
Oranges	1.55	.088	.040	.00039	.123	.091
Orange juice	1.44	.067	.037	.00046	.093	.082
Oysters	12.30	.106	.306	.00893	.149	.702
Parsnips	2.47	.091	.117	.0009	.128	.268
Peaches	1.70	.038	.057	.00073	.053	.130
Peanuts	4.70	.013	.073	.00036	.018	.166
Pears	0.95	.024	.041	.00047	.033	.093
Peas	6.92	.026	.120	.00165	.036	.274
Pecans	1.30	.012	.045	.00035	.017	.104
Pepper, green	4.59	.034	.145	.00222	.047	.333
Perch (See Fish)						
Persimmons	—	—	—	—	—	—
Pineapple, fresh	0.92	.041	.064	.00116	.058	.146

TABLE III — *Continued*

FOOD	PROTEIN	CALCIUM (Ca)	PHOSPHORUS (P)	IRON (Fe)	CaO	P_2O_5
	Grams	Grams	Grams	Grams	Grams	Grams
Plums	1.20	.024	.038	.00059	.033	.087
Pork (See Meat)						
Potatoes	2.65	.016	.069	.00156	.023	.158
sweet	1.45	.016	.037	.00041	.023	.084
Prunes	0.70	.018	.035	.00100	.025	.080
Pumpkin	3.90	.089	.229	(.00130)	.125	.525
Radishes	4.42	.073	.098	.00205	.102	.225
Raisins	0.75	.019	.038	.00139	.026	.088
Raspberries	2.57	.074	.078	.00091	.104	.178
Rhubarb	2.60	.189	.134	.00433	.264	.307
Rice, brown	2.52	(.003)	.060	.00058	(.004)	.138
white	2.27	$.001^+$	.027	.00026	.003	.063
Rutabagas	3.15	.185	.140	—	.259	.322
Rye, entire	—	—	—	—	—	—
Salmon (See Fish)						
Shredded wheat	3.50	.011	.089	.00123	.016	.203
Spinach	8.79	.281	.285	.01506	.393	.653
Squash, summer	3.05	.039	.035	(.0013)	.054	.080
winter	3.10	.040	.061	(.0013)	.056	.139
Strawberries	2.56	.104	.072	.00205	.146	.164
Tapioca	0.11	.004	.025	.00045	.006	.058
Tomatoes	3.95	.050	.113	.00175	.070	.259
Turnips	3.30	.161	.117	.00127	.226	.269
Turnip tops	—	—	—	—	—	—
Veal (See Meat)						
Vinegar (cider)	—	.111	.090	.00213	.156	.206
Walnuts, California or English	2.60	.013	.015	.00030	.018	.116
Water cress	—	—	—	—	—	—
Watermelon	1.32	.038	.010	(.00099)	.053	.023
Wheat, entire	3.63?	.013	.118	.00140	.018	.270
Wheat germ	—	—	—	—	—	—
Wheat gluten	—	—	—	—	—	—
Whey	3.74	.165	.131	?	.231	.300
Whortleberries	—	—	—	—	—	—
Wine (average, 10 per cent alcohol)	—	.011	.021	.00167	.016	.047

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